

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4379	zwf or (g6p or glc6p or glucose-6-phosphate) adj (dh or dehydrogenase\$1) or g6pdh	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:20
L2	11	1 same corynebacter\$	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:21
L3	13	1 same ((amino adj acid or lysine or threonine or tryptophan or lys or thr or trp) near4 (biosynthes\$ or synthes\$10 or prepar\$10))\	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:23
(L4)	20	2 or 3	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:23

PGPUB-DOCUMENT-NUMBER: 20040091976

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040091976 A1

TITLE: Process and materials for production of glucosamine and  
N-acetylglucosamine

PUBLICATION-DATE: May 13, 2004

INVENTOR-INFORMATION:

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Jerrell, Thomas A. JR.	Manitowoc	WI	US	
Leanna, Candice	Green Bay	WI	US	
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Rosson, Reinhardt	Manitowoc	WI	US	
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APPL-NO: 10/ 612779

DATE FILED: July 1, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60393348 20020701 US

US-CL-CURRENT: 435/84, 435/193 , 435/252.3

ABSTRACT:

A biosynthetic method for producing glucosamine and N-acetylglucosamine is disclosed. Such a method includes the fermentation of a genetically modified microorganism to produce glucosamine and/or N-acetylglucosamine. Also disclosed are genetically modified microorganisms that are useful for producing glucosamine and N-acetylglucosamine. In addition, methods of recovering N-acetylglucosamine that has been produced by a fermentation process, including methods that result in N-acetylglucosamine of high purity, are described. Also disclosed is a method to produce glucosamine from N-acetylglucosamine.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority under 35 U.S.C. .sctn. 119(e) from U.S. Provisional Application Serial No. 60/393,348, filed Jul. 1, 2002, entitled, "Process and Materials for Production of Glucosamine and N-Acetylglucosamine." The entire disclosure of U.S. Provisional Application Serial No. 60/393,348 is incorporated herein by reference.

----- KWIC -----

Detail Description Paragraph - DETX (578):

[0619] The pentose phosphate pathway provides intermediates for amino acid, nucleotides, and cell wall biosynthesis. Furthermore, the oxidative portion of the pentose phosphate pathway is an important source of NADPH in the cell. The zwf gene of *E. coli* encodes the glucose-6-phosphate dehydrogenase (G6PDH), which catalyzes the first step in the pentose phosphate pathway, converting glucose-6-phosphate into glucono-1,5-lactone. Expression of the zwf gene is coordinated with the cellular growth rate (Rowley, D. and Wolf, R., *J. Bac.*, 1991, 173(3):968-977).

PGPUB-DOCUMENT-NUMBER: 20040043458

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040043458 A1

TITLE: Coryneform bacteria which produce chemical compounds II

PUBLICATION-DATE: March 4, 2004

INVENTOR-INFORMATION:

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Mockel, Bettina	Dusseldorf		DE	
Thierbach, Georg	Bielefeld		DE	

APPL-NO: 10/ 358393

DATE FILED: February 5, 2003

RELATED-US-APPL-DATA:

child 10358393 A1 20030205

parent continuation-of PCT/EP02/08465 20020730 US UNKNOWN

non-provisional-of-provisional 60309877 20010806 US

US-CL-CURRENT: 435/91.1, 435/115, 435/252.3, 435/320.1, 435/471, 435/472  
, 435/66, 435/67

ABSTRACT:

The invention relates to coryneform bacteria which, instead of the singular copy of an open reading frame (ORF), gene or allele naturally present at the particular desired site (locus), have at least two copies of the open reading frame (ORF), gene or allele in question, preferably in tandem arrangement, and optionally at least a third copy of the open reading frame (ORF), gene or allele in question at a further gene site, and processes for the preparation of chemical compounds by fermentation of these bacteria.

[0001] This is a continuation of International Patent Appl. No. PCT/EP02/08465, filed Jul. 30, 2002, which claims priority to U.S. Prov. Appl. No. 60/309,877, filed Aug. 6, 2001.

----- KWIC -----

Claims Text - CLTX (30):

29. Process for the preparation of L-lysine according to claim 26, wherein the copy of an open reading frame (ORF), a gene or allele of lysine production is one or more of the open reading frames, genes or alleles chosen from the group consisting of accBC, accDA, cstA, cysD, cysE, cysH, cysK, cysN, cysQ, dapA, dapB, dapC, dapD, dapE, dapF, ddh, dps, eno, gap, gap2, gdh, gnd, lysC, lysC.sup.FBR, lysE, msik, opcA, oxyR, ppc, ppc.sup.FBR, pgk, pknA, pknB, pknD,

pknG, ppsA, ptsH, ptsI, ptsM, pyc, pyc P458S, sigC, sigD, sigE, sigH, sigM, tal, thyA, tkt, tpi, zwa1, zwf and zwf A213T.

PGPUB-DOCUMENT-NUMBER: 20030219881

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030219881 A1

TITLE: Coryneform bacteria which produce chemical compounds I

PUBLICATION-DATE: November 27, 2003

INVENTOR-INFORMATION:

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Bettina, Mockel	Dusseldorf		DE	
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APPL-NO: 10/ 358405

DATE FILED: February 5, 2003

RELATED-US-APPL-DATA:

child 10358405 A1 20030205

parent continuation-in-part-of PCT/EP02/08464 20020730 US UNKNOWN

non-provisional-of-provisional 60309878 20010806 US

US-CL-CURRENT: 435/106, 435/107 , 435/108 , 435/109 , 435/252.3 , 435/66  
, 435/67 , 435/91.1

ABSTRACT:

The invention relates to coryneform bacteria which have, in addition to at least one copy, present at the natural site (locus), of an open reading frame (ORF), gene or allele which codes for the synthesis of a protein or an RNA, in each case a second, optionally third or fourth copy of this open reading frame (ORF), gene or allele at in each case a second, optionally third or fourth site in a form integrated into the chromosome and processes for the preparation of chemical compounds by fermentation of these bacteria.

----- KWIC -----

Claims Text - CLTX (28):

27. Process for the preparation of L-lysine according to claim 26, wherein the open reading frame (ORF), gene or allele of lysine production is an open reading frame, a gene or allele chosen from the group consisting of accBC, accDA, cstA, cysD, cysE, cysH, cysK, cysN, cysQ, dapA, dapB, dapC, dapD, dapE, dapF, ddh, dps, eno, gap, gap2, gdh, gnd, lysC, lysC.sup.FBR, lysE, msiK, opcA, oxyR, ppc, ppc.sup.FBR, pgk, pknA, pknB, pknD, pknG, ppsA, ptsH, ptsI, ptsM, pyc, pyc P458S, sigC, sigD, sigE, sigH, sigM, tal, thyA, tkt, tpi, zwa1, zwf and zwf A213T.

PGPUB-DOCUMENT-NUMBER: 20030199045

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030199045 A1

TITLE: Process for the preparation of L-amino acids with  
amplification of the zwf gene

PUBLICATION-DATE: October 23, 2003

INVENTOR-INFORMATION:

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Burke, Kevin	Galway		IE	
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Moritz, Bernd	Niederzier		DE	
Dunican, L. K.	Galway		IE	
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Stapelton, Cliona	Roscrea		IE	
Mockel, Bettina	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	
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APPL-NO: 10/ 091342

DATE FILED: March 6, 2002

RELATED-US-APPL-DATA:

child 10091342 A1 20020306

parent continuation-in-part-of 09531269 20000320 US ABANDONED

US-CL-CURRENT: 435/115, 435/252.3 , 435/476

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids. The process involves fermenting an L-amino acid producing coryneform bacteria in a culture medium, concentrating L-amino acid in the culture medium or in the cells of the bacteria, and isolating the L-amino acid produced. The bacteria has an amplified gene encoding the Zwischenferment protein.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This is a continuation-in-part of U.S. application Ser. No. 09/531,269, filed Mar. 20, 2000, the contents of which are incorporated by reference herein in their entirety.

----- KWIC -----

Detail Description Paragraph - DETX (97):

[0107] Preparation of Amino Acid Producers with an Amplified zwf Gene

Detail Description Paragraph - DETX (134):

[0139] Effect of Over-Expression of the zwf Gene with Simultaneous

## Elimination of the pgi Gene on the Preparation of Lysine

Detail Description Paragraph - DETX (160):

[0160] Effect of Over-Expression of the zwf Gene with Simultaneous Elimination of the poxB Gene on the Preparation of Lysine

Claims Text - CLTX (2):

1. A process for the preparation of L-lysine comprising: a) fermenting an L-lysine producing coryneform bacteria in a culture medium, the bacteria having at least an overexpressed zwf gene encoding the Zwischenferment protein; b) concentrating the L-lysine in the culture medium or in the cells of the bacteria; and c) isolating the L-lysine produced; wherein intracellular activity of pyruvate oxidase encoded by the poxB gene is decreased or switched off in the bacteria.

Claims Text - CLTX (8):

7. A process for the preparation of L-lysine, comprising: a) fermenting an L-lysine producing bacteria in a culture medium, the bacteria having at least an overexpressed zwf gene encoding the Zwischenferment protein; b) concentrating the L-lysine in the culture medium or in the cells of the bacteria; and c) isolating the L-lysine produced; wherein intracellular activity of the glucose 6-phosphate isomerase encoded by the pgi gene is decreased or switched off in the bacteria.

Claims Text - CLTX (12):

11. A coryneform microorganism of the genus Corynebacterium, transformed by the introduction of the plasmid vector as claimed in claim 9, the microorganism additionally containing the zwf gene.



PGPUB-DOCUMENT-NUMBER: 20030175911

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175911 A1

TITLE: Process for the preparation of L-amino acids with  
amplification of the zwf gene

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hans, Stephen	Osnabruek		DE	
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Reth, Alexander	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	
Kreutzer, Caroline	Melle		DE	
Mockel, Bettina	Dusseldorf		DE	

APPL-NO: 10/ 336049

DATE FILED: January 3, 2003

RELATED-US-APPL-DATA:

child 10336049 A1 20030103

parent continuation-in-part-of 10091342 20020306 US PENDING

child 10091342 20020306 US

parent continuation-in-part-of 09531269 20000320 US ABANDONED

US-CL-CURRENT: 435/115, 435/252.3

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids by the fermentation of coryneform bacteria. The process involves: fermenting an L-amino acid-producing bacteria in which at least the zwf gene is amplified; concentrating the L-amino acid in the medium or in the cells of the bacteria; and isolating the L-amino acid produced.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a continuation-in-part of U.S. Ser. No. 10/091,342, filed on Mar. 6, 2002, which is a continuation-in-part of U.S. Ser. No. 09/531,269, filed Mar. 20, 2000.

----- KWIC -----

Detail Description Paragraph - DETX (37):

[0049] Genes encoding Zwf proteins from Gram-negative bacteria e.g., *Escherichia coli* or other Gram-positive bacteria, e.g., *Streptomyces* or *Bacillus*, may optionally be used to increase Zwf expression in Corynebacterium. Alleles of the zwf gene which result from the degeneracy of the genetic code or

due to sense mutations of neutral function can also be used. However, the use of endogenous genes, in particular endogenous genes from coryneform bacteria, is preferred. "Endogenous genes" or "endogenous nucleotide sequences" refers to genes or nucleotide sequences which are available in the population of a species.

Detail Description Paragraph - DETX (54):

[0066] Accordingly, the invention provides isolated coryneform bacteria or mutants comprising a polynucleotide encoding a Zwf protein comprising the amino acid sequence of SEQ ID NO: 10, wherein at least one or more of the amino acids at positions 369 to 373 and/or one or more of the amino acids at positions 241 to 246 is exchanged by another proteinogenic amino acid. Corynebacterium glutamicum DM658 is an example of such a coryneform bacterium. It was obtained after multiple rounds of mutagenesis, selection and screening and contains in its chromosome a zwf allele (zwf(A243T)) coding for a Zwf protein (Zwf(A243T)) having the amino acid sequence of SEQ ID NO: 10 wherein L-alanine at position 243 is replaced by L-threonine as is shown in SEQ ID NO: 22.

Detail Description Paragraph - DETX (56):

[0068] The corresponding alleles or mutations are sequenced and introduced by recombination into the chromosome of an appropriate strain by the method of gene replacement, for example as described by Schwarzer, et al. (Bio/Technology 9:84-87 (1991)) for the lysA gene of C. glutamicum or by Peters-Wendisch, et al. (Microbiology 144:915-927 (1998)) for the pyc gene of C. glutamicum. Corynebacterium glutamicum DSM5715zwf2\_A243T is an example for such a strain. It comprises in its chromosome the mutation of the zwf allele of strain DM658, i.e. zwf(A243T).

Detail Description Paragraph - DETX (57):

[0069] The corresponding alleles can also be introduced into the chromosome of an appropriate strain by the method of gene duplication, for example as described by Reinscheid, et al. (Appl. Environ. Microbiol. 60(1):126-132 (1994)) for the hom-thrB operon or by Jetten, et al. (Appl. Microbiol. Biotech. 43:76-82 (1995)) for the ask gene. Accordingly, the invention further provides coryneform bacteria comprising an isolated polynucleotide encoding a Zwf protein comprising the amino acid sequence of SEQ ID NO: 10, wherein at least one or more of the amino acids at positions 369 to 373 and/or one or more of the amino acids at positions 241 to 246 is exchanged by another proteinogenic amino acid. Corynebacterium glutamicum DSM5715::pK18-mobsacB\_ zwf(A243T) is an example of such a strain. It comprises in its chromosome an isolated DNA containing the zwf(A243T) allele.

Detail Description Paragraph - DETX (59):

[0071] The strains thus obtained are used for the fermentative production of amino acids. In addition, it may be advantageous for the production of L-amino acids to amplify one or more enzymes of the particular biosynthesis pathway, of glycolysis, of anaplerosis, of the pentose phosphate pathway or of amino acid export, in addition to amplification of the zwf gene. Thus, for the preparation of L-threonine, one or more genes chosen from the following group may be can be amplified, in particular over-expressed, at the same time:

Detail Description Paragraph - DETX (115):

[0125] The zwf gene from Corynebacterium glutamicum ATCC13032 was first amplified by a polymerase chain reaction (PCR) by means of the following oligonucleotide primers:

Detail Description Paragraph - DETX (120):

[0129] Preparation of Amino Acid Producers with an Amplified zwf Gene

Detail Description Paragraph - DETX (162):

[0166] Effect of Over-Expression of the zwf Gene with Simultaneous Elimination of the pgi Gene on the Preparation of Lysine

Detail Description Paragraph - DETX (192):

[0191] Effect of Over-Expression of the zwf Gene with Simultaneous Elimination of the poxB Gene on the Preparation of Lysine

Claims Text - CLTX (2):

1. A process for the preparation of L-lysine by the fermentation of bacteria comprising the following steps: a) fermenting L-lysine producing bacteria in which a zwf gene encoding the Zwischenferment protein is overexpressed relative to the wild-type bacteria; b) concentrating L-lysine in the medium or in the cells of said coryneform bacteria; and c) isolating the L-lysine produced; wherein the intracellular activity of pyruvate oxidase encoded by the poxB gene is decreased or switched off.

Claims Text - CLTX (8):

7. A process for the preparation of L-lysine by fermentation of coryneform bacteria comprising the following steps: a) fermenting L-lysine producing bacteria in which a zwf gene encoding the Zwischenferment protein is overexpressed relative to the wild-type bacteria; b) concentrating the L-lysine in the medium or in the cells of the bacteria; and c) isolating the L-lysine produced; wherein the intracellular activity of the glucose 6-phosphate isomerase encoded by the pgi gene is decreased or switched off.

Claims Text - CLTX (54):

53. A process for the preparation of an amino acid by fermentation of an isolated coryneform bacterium comprising the following steps: a) fermenting an amino acid producing bacterium comprising a polynucleotide encoding a protein having glucose-6-phosphate dehydrogenase activity comprising at least the amino acid sequence of SEQ ID NO: 22 positions 241 to 246, and b) concentrating of the amino acid in the medium or in the cells of the bacterium.

Claims Text - CLTX (55):

54. A process for the preparation of an amino acid by fermentation of a coryneform bacterium comprising the following steps: a) fermenting an amino acid producing bacterium comprising an isolated polynucleotide encoding a protein having glucose-6-phosphate dehydrogenase activity with at least the amino acid sequence of SEQ ID NO: 22 positions 241 to 246, and b) concentrating of the amino acid in the medium or in the cells of the bacterium.

PGPUB-DOCUMENT-NUMBER: 20030138917

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030138917 A1

TITLE: Nucleotide sequences which code for the opcA gene

PUBLICATION-DATE: July 24, 2003

INVENTOR-INFORMATION:

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Dunican, Rita	Galway		IE	
McCormack, Ashling	County Westmeath		IE	
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Burke, Kevin	County Galway		IE	
Moritz, Bernd S.	Niederzier		DE	
Eggeling, Lothar	Julich		DE	
Sahm, Hermann	Julich		DE	
Mockel, Bettina	Bielefeld		DE	
Weissenborn, Anke	Tubingen		DE	

APPL-NO: 10/ 137655

DATE FILED: May 3, 2002

RELATED-US-APPL-DATA:

child 10137655 A1 20020503

parent continuation-in-part-of 09531267 20000320 US ABANDONED

non-provisional-of-provisional 60142915 19990709 US

US-CL-CURRENT: 435/106, 435/115, 435/191, 435/193, 435/194, 435/252.3  
, 435/320.1, 435/69.1, 435/91.2

ABSTRACT:

The present invention relates to polynucleotides that encode proteins having OpcA enzymatic activity. These polynucleotides can be used for increasing lysine biosynthesis in Coryneform glutamicum.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a continuation-in-part of U.S. application Ser. No. 09/531,267 filed on Mar. 20, 2000, which, in turn, claims the benefit of U.S. Provisional Application No. 60/142,915 filed on Jul. 9, 1999. The contents of U.S. application Ser. No. 09/531,267 are incorporated herein by reference in their entirety.

----- KWIC -----

Detail Description Paragraph - DETX (136):  
Purification and N-terminal Sequencing of the Glucose-6-Phosphate Dehydrogenase of Corynebacterium glutamicum ATCC13032.

Detail Description Paragraph - DETX (138):

[0170] For purification of the glucose-6-phosphate dehydrogenase Corynebacterium glutamicum ATCC 13032 was grown aerobically on minimal medium at 30.degree. C. in a Labfors fermentation system (Infors AG, Bottmingen, Switzerland). A preculture (Bacto.RTM. Brain Heart Infusion medium, Difco Laboratories, Detroit, USA) was incubated for 15 hours at 30.degree. C. and used for inoculation of 2.5l minimal medium. The medium contained the following constituents (amounts per liter): 20 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>; 1 g KH<sub>2</sub>PO<sub>4</sub>; 1 g K<sub>2</sub>HPO<sub>4</sub>; 0.25 g MgSO<sub>4</sub>·7H<sub>2</sub>O; 10 mg CaCl<sub>2</sub>; 0.2 mg biotin; 30 mg protocatechuic acid; 1 mg FeSO<sub>4</sub>·7H<sub>2</sub>O; 1 mg MnSO<sub>4</sub>·H<sub>2</sub>O; 0.1 mg ZnSO<sub>4</sub>·7H<sub>2</sub>O; 0.02 mg CuSO<sub>4</sub>; 0.002 mg NiCl<sub>2</sub>·6H<sub>2</sub>O; 1.2 g HCl; 0.2 g polypropylene glycol; 75 mg tritriplex II and 100 g glucose. During fermentation sodium hydroxide was continuously added in order to keep the pH-value constant at 7.0. The cells were harvested in the late exponential growth phase. After centrifugation using an Avanti J-25 centrifuge and a JA10 rotor of Beckman (Fullerton, USA) at 6400 g for 15 minutes at 4.degree. C. and washing in 100 mM TRIS-HCl pH 7.5 containing 10 mM MgCl<sub>2</sub> the sediment was stored at -20.degree. C. until use.

Detail Description Paragraph - DETX (153):

[0183] PCR was used to amplify DNA fragments containing the entire zwf and opcA genes of C. glutamicum ATCC13032 and flanking upstream and downstream regions. PCR reactions were carried out using oligonucleotide primers designed from SEQ ID NO 1 and SEQ ID NO 6. Genomic DNA was isolated from Corynebacterium glutamicum ATCC13032 according to Heery and Dunican (Applied and Environmental Microbiology. 59: 791-799 (1993)) and used as template. The primers used were:

Detail Description Paragraph - DETX (170):

Expression of Glucose-6-Phosphate Dehydrogenase in Corynebacterium glutamicum

Detail Description Paragraph - DETX (171):

[0197] The entire zwf and opcA genes were subsequently isolated from the pGEM T-vector containing these genes (see Example 6) on an SphI/SalI fragment and cloned into the lacZ.alpha. SphI/SalI sites of the E. coli-C. glutamicum shuttle vector pEC-T18mob2 (see Example 7 and FIG. 2). This shuttle vector contains two SphI sites. The first is situated within the multiple cloning site of lacZ.alpha. and the second is situated within the gene conferring tetracycline resistance. Tetracycline (Sigma-Aldrich, PO Box 2424, Wimbome, Dorset BH21 7YR, UK) (5 mg/l) was used therefore as a selective pressure as only those clones containing the intact tetracycline resistance gene would grow. This new construct was designated pECzwfopcA (FIG. 3). Restriction enzyme analysis with SacI (Boehringer Mannheim GmbH, Germany) revealed the correct orientation of the zwf and opcA genes in the lacZ.alpha. gene of pEC-T18mob2 i.e. downstream the lac promoter. Corynebacterium glutamicum ATCC13032 (American Type Culture Collection, Manassas, Va., USA) was transformed with this construct and electrotransformants were selected on Luria agar supplemented with isopropyl-thiogalactopyranoside (IPTG), 5-bromo-4-chloro-3-indolyl-galactopyranoside (XGAL) and tetracycline at concentrations of 1 mM, 0.02% and 5 mg/l respectively. Agar plates were incubated for 48 hours at 30.degree. C. Rapid plasmid preparations were carried out as described by O'Gara and Dunican, (Applied and Environmental Microbiology 61: 4477-4479 (1995)), and Sac I restriction confirmed the presence of required clones. One of the clones was designated ATCC13032/pECzwfopcA.

Claims Text - CLTX (12):

11. The process as claimed in claim 8, wherein for the preparation of amino acids, in particular lysine, bacteria in which, in addition to the opcA gene, one or more genes chosen from the group consisting of 11.1 the dapA gene which codes for dihydrodipicolinate synthase, 11.2 the lysC gene which codes for a feed back resistant aspartate kinase, 11.3 the gap gene which codes for glycerolaldehyde 3-phosphate dehydrogenase, 11.4 the pyc gene which codes for pyruvate carboxylase, 11.5 the tkt gene which codes for transketolase, 11.6 the gnd gene which codes for 6-phosphogluconate dehydrogenase, 11.7 the lysE gene which codes for lysine export protein, 11.8 the zwa1 gene, 11.9 the eno gene which codes for enolase, 11.10 the tal gene which codes for transaldolase, 11.11 in particular the zwf gene is or are amplified, in particular over-expressed, at the same time, are fermented.

PGPUB-DOCUMENT-NUMBER: 20030135878

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030135878 A1

TITLE: Transgenic plants with elevated thioredoxin levels

PUBLICATION-DATE: July 17, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cho, Myeong-Je	Alameda	CA	US	
Wong, J. H.	San Francisco	CA	US	
Lemaux, Peggy G.	Moraga	CA	US	
Buchanan, Bob B.	Berkeley	CA	US	

APPL-NO: 10/ 194885

DATE FILED: July 12, 2002

RELATED-US-APPL-DATA:

child 10194885 A1 20020712

parent continuation-in-part-of 09538864 20000329 US PENDING

non-provisional-of-provisional 60307006 20010719 US

non-provisional-of-provisional 60126736 19990329 US

US-CL-CURRENT: 800/278, 800/320 , 800/320.1 , 800/320.2 , 800/320.3

ABSTRACT:

The present invention is directed to a transgenic plant wherein at least a part of said plant includes a recombinant nucleic acid with a promoter active in the part operably linked to a nucleic acid encoding a thioredoxin polypeptide wherein the promoter is a seed or grain maturation-specific promoter and the thioredoxin polypeptide includes the amino acid sequence WCGPC. The present invention is further directed to transgenic plants that overexpress thioredoxin in seed wherein the overexpression of thioredoxin h effects a significant increase in the reduction of proteins (--SH as compared to S--S) of the albumin fraction of the seed.

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application No. 60/307,006 filed Jul. 19, 2001 and is a continuation-in-part application of U.S. application Ser. No. 09/538,864 filed Mar. 29, 2000 which claims priority to U.S. Provisional Patent application No. 60/126,736 filed Mar. 29, 1999 all of which are hereby incorporated by reference in their entirety.

----- KWIC -----

Detail Description Paragraph - DETX (14):

[0076] Glucose-6-phosphate dehydrogenase: The term glucose-6-phosphate

dehydrogenase, (G6PDH) refers to an enzyme that catalyzes the first step of the oxidative pentose phosphate pathway (OPPP), namely the conversion of glucose-6-phosphate to 6-phosphogluconolactone. Concomitantly, NADPH is generated. The main function of G6PDH is to generate NADPH for anabolic metabolism, including fatty acid, amino acid and ribose synthesis. G6PDH includes those sequences described in FIG. 31 and homologues thereof.

Detail Description Paragraph - DETX (350):

[0388] The driving force of the reaction is the source of electrons, NADPH. This coenzyme can be generated through glucose-6-phosphate dehydrogenase (G6DPH), which catalyzes the first step of the oxidative pentose phosphate pathway (OPPP), namely the conversion of glucose-6-phosphate to 6-phosphogluconolactone. Concomitantly, NADPH is generated. The main function of G6PDH is to generate NADPH for anabolic metabolism, including fatty acid synthesis, amino acid, and ribose synthesis (Copeland and Turner, 1987; Turner and Turner, 1980; Dennis et al., 1997).



PGPUB-DOCUMENT-NUMBER: 20030109014

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109014 A1

TITLE: Process for the fermentative preparation of L-amino acids with amplification of the tkt gene

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Burke, Kevin	Newcastle		IE	
Duncan, L. K.	Bushy Park		IE	
Duncian, Rita	Galway		IE	
McCormack, Ashling	Athlone		IE	
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Mockel, Bettina	Bielefeld		DE	
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APPL-NO: 10/ 143856

DATE FILED: May 14, 2002

RELATED-US-APPL-DATA:

child 10143856 A1 20020514

parent continuation-in-part-of 09986649 20011109 US ABANDONED

child 09986649 20011109 US

parent continuation-in-part-of 09528196 20000317 US ABANDONED

US-CL-CURRENT: 435/115, 435/106 , 435/189 , 435/193 , 435/252.3 , 435/320.1 , 435/69.1 , 536/23.2

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids by the fermentation of coryneform bacteria that over-express a gene encoding transketolase.

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application is a continuation-in-part of U.S. application Ser. No. 09/986,649, filed Nov. 9, 2001, which is a continuation-in-part of U.S. application Ser. No. 09/528,196, filed Mar. 17, 2000.

----- KWIC -----

Claims Text - CLTX (3):

2. The process of claim 1, wherein said process is for the preparation of L-lysine and, in addition to over-expressing said endogenous gene coding for tkt, said bacteria have at least one additional endogenous gene that is over-expressed or amplified, said additional endogenous gene being selected from

the group consisting of: (a) the dapA gene which codes for dihydrodipicolinate synthase; (b) the lysC gene which codes for a feedback resistant aspartate kinase; (c) the gap gene which codes for glycerolaldehyde 3-phosphate dehydrogenase; (d) the pyc gene which codes for pyruvate carboxylase; (e) the zwf gene which codes for glucose 6-phosphate dehydrogenase; (f) the gnd gene which codes for 6-phosphogluconate dehydrogenase; (g) the lysE gene which codes for lysine export protein; (h) the mqo gene which codes for malate-quinone oxidoreductase; and the eno gene which codes for enolase.

Claims Text - CLTX (4):

3. The process of claim 1, wherein said process is for the preparation of L-threonine and, in addition to over-expressing said endogenous gene coding for tkt, said bacteria have at least one additional endogenous gene that is over-expressed or amplified, said additional endogenous gene being selected from the group consisting of: the hom gene which codes for homoserine dehydrogenase; the hom.sup.dr allele which codes for a "feed back resistant" homoserine dehydrogenase; (c) the gap gene which codes for glycerolaldehyde 3-phosphate dehydrogenase; (d) the pyc gene which codes for pyruvate carboxylase; (e) the mqo gene which codes for malate:quinone oxidoreductase; (f) the zwf gene which codes for glucose 6-phosphate dehydrogenase; (g) the gnd gene which codes for 6-phosphogluconate dehydrogenase; (h) the thrE gene which codes for threonine export protein; and (i) the eno gene which codes for enolase.

PGPUB-DOCUMENT-NUMBER: 20030100080

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030100080 A1

TITLE: Nucleotide sequences which code for the sahH gene

PUBLICATION-DATE: May 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
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Huthmacher, Klaus	Gelnhausen		DE	
Brehme, Jennifer	Bielefeld		DE	
Pfefferle, Walter	Halle		DE	
Binder, Michael	Steinhagen		DE	
Greissinger, Dieter	Niddatal		DE	
Thierbach, Georg	Bielefeld		DE	

APPL-NO: 09/ 919854

DATE FILED: August 2, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60294277 20010531 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	DE 100 44 706.6	2000DE-DE 100 44 706.6	September 9, 2000
DE	DE 101 09 685.2	2001DE-DE 101 09 685.2	February 28, 2001

US-CL-CURRENT: 435/106, 435/252.33 , 435/320.1 , 435/69.1 , 536/23.2

ABSTRACT:

An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of

- polynucleotide which is at least 70% identical to a polynucleotide that codes for a polypeptide which comprises the amino acid sequence of SEQ ID No. 2,
- polynucleotide which codes for a polypeptide that comprises an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID No. 2,
- polynucleotide which is complementary to the polynucleotides of a) or b), and
- polynucleotide comprising at least 15 successive nucleotides of the polynucleotide sequence of a), b) or c),

and a process for the fermentative preparation of L-amino acids using coryneform bacteria, in which at least the sahH gene is present in enhanced form, and the use of polynucleotides which contain the sequences according to the invention as hybridization probes.

----- KWIC -----

Claims Text - CLTX (16):

16. The process as claimed in claim 10, wherein for the preparation of L-lysine or L-methionine the coryneform microorganisms have one or more enhanced genes selected from the group consisting of 16.1 the dapA gene which codes for dihydrodipicolinate synthase, 16.2 the gap gene which codes for glyceraldehyde 3-phosphate dehydrogenase, 16.3 the tpi gene which codes for triose phosphate isomerase, 16.4 the pgk gene which codes for 3-phosphoglycerate kinase, 16.5 the zwf gene which codes for glucose 6-phosphate dehydrogenase, 16.6 the pyc gene which codes for pyruvate carboxylase, 16.7 the mqo gene which codes for malate-quinone oxidoreductase, 16.8 the lysC gene which codes for a feed-back resistant aspartate kinase, 16.9 the lysE gene which codes for lysine export, 16.10 the hom gene which codes for homoserine dehydrogenase 16.11 the ilvA gene which codes for threonine dehydratase or the ilvA(Fbr) allele which codes for a feed back resistant threonine dehydratase, 16.12 the ilvBN gene which codes for acetohydroxy-acid synthase, 16.13 the ilvD gene which codes for dihydroxy-acid dehydratase, 16.14 the zwa1 gene which codes for the Zwa1 protein.

PGPUB-DOCUMENT-NUMBER: 20030049804

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030049804 A1

TITLE: Corynebacterium glutamicum genes encoding metabolic pathway proteins

PUBLICATION-DATE: March 13, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Pompejus, Markus	Freinsheim		DE	
Kroger, Burkhard	Limburgerhof		DE	
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Zelder, Oskar	Speyer		DE	
Haberhauer, Gregor	Limburgerhof		DE	
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Lee, Heung-Shick	Seoul		KR	
Hwang, Byung-Joon	Seoul		KR	

APPL-NO: 09/ 746660

DATE FILED: December 22, 2000

RELATED-US-APPL-DATA:

child 09746660 A1 20001222

parent continuation-in-part-of 09606740 20000623 US PENDING

child 09746660 A1 20001222

parent continuation-in-part-of 09603124 20000623 US PENDING

non-provisional-of-provisional 60141031 19990625 US

non-provisional-of-provisional 60142101 19990702 US

non-provisional-of-provisional 60148613 19990812 US

non-provisional-of-provisional 60187970 20000309 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	19931420.9	1999DE-19931420.9	July 8, 1999

US-CL-CURRENT: 435/115, 435/183, 435/252.3, 435/320.1, 435/69.1, 536/23.2

ABSTRACT:

Isolated nucleic acid molecules, designated MP nucleic acid molecules, which encode novel MP proteins from Corynebacterium glutamicum are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing MP nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further

provides isolated MP proteins, mutated MP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of MP genes in this organism.

#### RELATED APPLICATIONS

[0001] The present application is an continuation in part of U.S. patent application Ser. No. 09/606,740, filed Jun. 23, 2000. This application is also a continuation in part of U.S. patent application Ser. No. 09/603,124, filed Jun. 23, 2000. The present application claims priority to prior filed U.S. Provisional Patent Application Serial No. 60/141031, filed Jun. 25, 1999, U.S. Provisional Patent Application Serial No. 60/142101, filed Jul. 2, 1999, U.S. Provisional Patent Application Serial No. 60/148613, filed Aug. 12, 1999, U.S. Provisional Patent Application Serial No. 60/187970, filed Mar. 9, 2000, and also to German Patent Application No. 19931420.9, filed Jul. 8, 1999. The entire contents of all of the aforementioned applications are hereby expressly incorporated herein by this reference.

----- KWIC -----

Detail Description Table CWU - DETL (6):

A 1 03/08/94 E07701 secY Honno, N. et al. "Gene DNA participating in integration of membraneous protein to membrane," Patent: JP 1994169780-A 1 06/21/94 E08177 Aspartokinase Sato, Y. et al. "Genetic DNA capable of coding Aspartokinase released from feedback inhibition and its utilization," Patent: JP 1994261766-A 1 09/20/94 E08178, Feedback inhibition-released Sato, Y. et al. "Genetic DNA capable of coding Aspartokinase released from E08179, Aspartokinase feedback inhibition and its utilization," Patent: JP 1994261766-A 1 09/20/94 E08180, E08181, E08182 E08232 Acetohydroxy-acid isomeroreductase Inui, M. et al. "Gene DNA coding acetohydroxy acid isomeroreductase," Patent: JP 1994277067-A 1 10/04/94 E08234 secE Asai, Y. et al. "Gene DNA coding for translocation machinery of protein," Patent: JP 1994277073-A 1 10/04/94 E08643 FT aminotransferase and Hatakeyama, K. et al. "DNA fragment having promoter function in desthiobiotin synthetase promoter coryneform bacterium," Patent: JP 1995031476-A 1 02/03/95 region E08646 Biotin synthetase Hatakeyama, K. et al. "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031476-A 1 02/03/95 E08649 Aspartase Kohama, K. et al. "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031478-A 1 02/03/95 E08900 Dihydrodipicolinate reductase Madori, M. et al. "DNA fragment containing gene coding Dihydro- dipicolinate acid reductase and utilization thereof," Patent: JP 1995075578-A 1 03/20/95 E08901 Diaminopimelic acid decarboxylase Madori, M. et al. "DNA fragment containing gene coding Diaminopimelic acid decarboxylase and utilization thereof," Patent: JP 1995075579- A 1 03/20/95 E12594 Serine hydroxymethyltransferase Hatakeyama, K. et al. "Production of L-tryptophan," Patent: JP 1997028391- A 1 02/04/97 E12760, transposase Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: E12759, JP 1997070291-A 03/18/97 E12758 E12764 Arginyl-tRNA synthetase; diamino- Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: pimelic acid decarboxylase JP 1997070291-A 03/18/97 E12767 Dihydrodipicolinic acid synthetase Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97 E12770 aspartokinase Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97 E12773 Dihydrodipicolinic acid reductase Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97 E13655 Glucose-6-phosphate dehydrogenase Hatakeyama, K. et al. "Glucose-6-phosphate dehydrogenase and DNA capable of coding the same," Patent: JP 1997224661-A 1 09/02/97 L01508 IlvA

Threonine dehydratase Moeckel, B. et al. "Functional and structural analysis of the threonine dehydratase of Corynebacterium glutamicum," J. Bacteriol., 174:8065-8072 (1992) L07603 EC 4.2.1.15 3-deoxy-D-arabinoheptulosonate-7-phosphate synthase glutamicum 3-deoxy-D-arabinoheptulosonate-7-phosphate synthase gene," FEMS Microbiol. Lett., 107:223-230 (1993) L09232 ilvB; ilvN; ilvC Acetohydroxy acid synthase large Keilhauer, C. et al. "Isoleucine synthesis in Corynebacterium glutamicum: subunit; Acetohydroxy acid synthase molecular analysis of the ilvB-ilvN-ilvC operon," J. Bacteriol., 175(17): small subunit; Acetohydroxy acid 5595-5603 (1993) isomeroreductase L18874 PtsM Phosphoenolpyruvate sugar Fouet, A et al. "Bacillus subtilis sucrose-specific enzyme II of the phosphotransferase phosphotransferase system: expression in Escherichia coli and homology to enzymes II from enteric bacteria," PNAS USA, 84(24): 8773-8777 (1987); Lee, J. K. et al. "Nucleotide sequence of the gene encoding the Corynebacterium glutamicum mannose enzyme II and analyses of the deduced protein sequence," FEMS Microbiol. Lett., 119(1-2): 137-145 (1994) L27123 aceB Malate synthase Lee, H-S. et al. "Molecular characterization of aceB, a gene encoding malate synthase in Corynebacterium glutamicum," J. Microbiol. Biotechnol., 4(4): 256-263 (1994) L27126 Pyruvate kinase Jetten, M. S. et al. "Structural and functional analysis of pyruvate kinase from Corynebacterium glutamicum," Appl. Environ. Microbiol., 60(7): 2501-2507 (1994) L28760 aceA Isocitrate lyase L35906 dtxR Diphtheria toxin repressor Oguiza, J. A. et al. "Molecular cloning, DNA sequence analysis, and characterization of the Corynebacterium diphtheriae dtxR from Brevibacterium lactofermentum," J. Bacteriol., 177(2): 465-467 (1995) M13774 Prephenate dehydratase Follettie, M. T. et al. "Molecular cloning and nucleotide sequence of the Corynebacterium glutamicum pheA gene," J. Bacteriol., 167: 695-702 (1986) M16175 5S rRNA Park, Y-H. et al. "Phylogenetic analysis of the coryneform bacteria by 56 rRNA sequences," J. Bacteriol., 169: 1801-1806 (1987) M16663 trpE Anthranilate synthase, 5' end Sano, K. et al. "Structure and function of the trp operon control regions of Brevibacterium lactofermentum, a glutamic-acid-producing bacterium," Gene, 52:191-200 (1987) M16664 trpA Tryptophan synthase, 3' end Sano, K. et al. "Structure and function of the trp operon control regions of Brevibacterium lactofermentum, a glutamic-acid-producing bacterium," Gene, 52: 191-200 (1987) M25819 Phosphoenolpyruvate carboxylase O'Regan, M. et al. "Cloning and nucleotide sequence of the Phosphoenolpyruvate carboxylase-coding gene of Corynebacterium glutamicum ATCC 13032," Gene, 77(2): 237-251 (1989) M85106 23S rRNA gene insertion sequence Roller, C. et al. "Gram-positive bacteria with a high DNA G+C content are characterized by a common insertion within their 23S rRNA genes," J. Gen. Microbiol., 138: 1167-1175 (1992) M85107, 23S rRNA gene insertion sequence Roller, C. et al. "Gram-positive bacteria with a high DNA G+C content are M85108 characterized by a common insertion within their 23S rRNA genes," J. Gen. Microbiol., 138: 1167-1175 (1992) M89931 aecD; brnQ; Beta C-S lyase; branched-chain Rossol, I. et al. "The Corynebacterium glutamicum aecD gene encodes a C-S yhbw amino acid uptake carrier; lyase with alpha, beta-elimination activity that degrades aminoethylcysteine," hypothetical protein yhbw J. Bacteriol., 174(9): 2968-2977 (1992); Tauch, A. et al. "Isoleucine uptake in Corynebacterium glutamicum ATCC 13032 is directed by the brnQ gene product," Arch. Microbiol., 169(4): 303-312 (1998) S59299 trp Leader gene (promoter) Herry, D. M. et

PGPUB-DOCUMENT-NUMBER: 20020197605

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020197605 A1

TITLE: Novel Polynucleotides

PUBLICATION-DATE: December 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nakagawa, Satoshi	Tokyo		JP	
Mizoguchi, Hiroshi	Tokyo		JP	
Ando, Seiko	Tokyo		JP	
Hayashi, Mikiro	Tokyo		JP	
Ochiai, Keiko	Tokyo		JP	
Yokoi, Haruhiko	Tokyo		JP	
Tateishi, Naoko	Tokyo		JP	
Senoh, Akihiro	Tokyo		JP	
Ikeda, Masato	Tokyo		JP	
Ozaki, Akio	Hofu-shi		JP	

APPL-NO: 09/ 738626

DATE FILED: December 18, 2000

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	P. HEI 11-377484	1999JP-P. HEI 11-377484	December 16, 1999
JP	P. 2000-159162	2000JP-P. 2000-159162	April 7, 2000
JP	P. 2000-280988	2000JP-P. 2000-280988	August 3, 2000

US-CL-CURRENT: 435/6, 435/287.2 , 435/91.2

ABSTRACT:

Novel polynucleotides derived from microorganisms belonging to coryneform bacteria and fragments thereof, polypeptides encoded by the polynucleotides and fragments thereof, polynucleotide arrays comprising the polynucleotides and fragments thereof, recording media in which the nucleotide sequences of the polynucleotide and fragments thereof have been recorded which are readable in a computer, and use of them.

----- KWIC -----

Detail Description Paragraph - DETX (584):

[0599] Corynebacterium glutamicum B-6, which is resistant to S-(2-aminoethyl)cysteine (AEC), rifampicin, streptomycin and 6-azauracil, is a lysine-producing mutant having been mutated and bred by subjecting the wild type ATCC 13032 strain to multiple rounds of random mutagenesis with a mutagen, N-methyl-N'-nitro-N-nitrosoguanidine (NTG) and screening (Appl. Microbiol. Biotechnol., 32:269-273 (1989)). First, the nucleotide sequences of genes derived from the B-6 strain and considered to relate to the lysine production were determined by a method similar to the above. The genes relating to the lysine production include lyse and lysG which are lysine-excreting genes; ddh, dapA, hom and lysC (encoding diaminopimelate dehydrogenase, dihydropicolinate



synthase, homoserine dehydrogenase and aspartokinase, respectively) which are lysine-biosynthesis genes; and pyc and zwf (encoding pyruvate carboxylase and glucose-6-phosphate dehydrogenase, respectively) which are glucose-metabolizing genes. The nucleotide sequences of the genes derived from the production strain were compared with the corresponding nucleotide sequences of the ATCC 13032 strain genome represented by SEQ ID NOS:1 to 3501 and analyzed. As a result, mutation points were observed in many genes. For example, no mutation site was observed in lysE, lysG, ddh, dapA, and the like, whereas amino acid replacement mutations were found in hom, lysC, pyc, zvf, and the like. Among these mutation points, those which are considered to contribute to the production were extracted on the basis of known biochemical or genetic information. Among the mutation points thus extracted, a mutation, Val59Ala, in hor and a mutation, Pro458Ser, in pyc were evaluated whether or not the mutations were effective according to the following method.

PGPUB-DOCUMENT-NUMBER: 20020168732

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168732 A1

TITLE: Process for the fermentative preparation of L-amino acids using coryneform bacteria

PUBLICATION-DATE: November 14, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Moeckel, Bettina	Duesseldorf		DE	
Hermann, Thomas	Bielefeld		DE	
Pfefferle, Walter	Halle	DE		

APPL-NO: 09/ 816079

DATE FILED: March 26, 2001

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 55 871.2	2000DE-100 55 871.2	November 10, 2000
DE	101 10 344.1	2001DE-101 10 344.1	March 3, 2001

US-CL-CURRENT: 435/115, 435/252.3

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids in which the following steps are carried out,  
a) fermentation of the coryneform bacteria which produce the desired L-amino acid and in which at least the nadA and/or nadC gene is or are attenuated,  
b) concentration of the desired L-amino acid in the medium or in the cells of the bacteria, and  
c) isolation of the L-amino acid,  
and optionally bacteria in which further genes of the biosynthesis pathway of the desired L-amino acid are additionally enhanced are employed, or bacteria in which the metabolic pathways which reduce the formation of the desired L-amino acid are at least partly eliminated are employed.

----- KWIC -----

Claims Text - CLTX (6):

6. A process as claimed in claim 1, wherein for the preparation of L-lysine, coryneform microorganisms in which at the same time one or more of the genes chosen from the group consisting of 6.1 the lysC gene which codes for a feed-back resistant aspartate kinase, 6.2 the dapA gene which codes for dihydrodipicolinate synthase, 6.3 the gap gene which codes for glyceraldehyde 3-phosphate dehydrogenase, 6.4 the pyc gene which codes for pyruvate carboxylase, 6.5 the mqo gene which codes for malate:quinone oxidoreductase, 6.6 the zwf gene which codes for glucose 6-phosphate dehydrogenase, 6.7 at the same time the lysE gene which codes for lysine export, 6.8 the zwa1 gene which codes for the Zwa1 protein 6.9 the tpi gene which codes for triose phosphate isomerase, and 6.10 the pgk gene which codes for 3-phosphoglycerate kinase, is or are enhanced, in particular over-expressed, are fermented.



PGPUB-DOCUMENT-NUMBER: 20020042105

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020042105 A1

TITLE: Nucleotide sequences coding for the pknB gene

PUBLICATION-DATE: April 11, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bathe, Brigitte	Saltzkotten		DE	
Hans, Stephan	Osnabrueck		DE	
Farwick, Mike	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	

APPL-NO: 09/ 949970

DATE FILED: September 12, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60297250 20010612 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 44 912.3	2000DE-100 44 912.3	September 12, 2000
DE	101 20 095.1	2001DE-101 20 095.1	April 25, 2001

US-CL-CURRENT: 435/106, 435/183, 435/252.3, 435/320.1, 536/23.2

ABSTRACT:

An isolated polynucleotide which contains a polynucleotide sequence selected from the group comprising:

- (a) a polynucleotide which is at least 70% identical to a polynucleotide coding for a polypeptide containing the amino acid sequence of SEQ ID No. 2,
  - (b) a polynucleotide coding for a polypeptide containing an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID No. 2,
  - (c) a polynucleotide which is complementary to the polynucleotides of (a) or (b), and
  - (d) a polynucleotide containing at least 15 consecutive nucleotides of the polynucleotide sequence of (a), (b) or (c),
- and a fermentation process for the preparation of L-amino acids using corynebacteria in which at least the pknB gene is amplified, and to the use, as hybridization probes, of polynucleotides containing the sequences according to the invention.

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims benefit to U.S. Provisional Application Ser. No. 60/297,250, filed on Jun. 12, 2001, and incorporated herein by reference.

----- KWIC -----

Claims Text - CLTX (26):

25. The process of claim 15, wherein one or more genes selected from the following group are simultaneously amplified or overexpressed in the corynebacteria: the dapA gene coding for dihydrodipicolinate synthase, the gap gene coding for glyceraldehyde 3-phosphate dehydrogenase, the tpi gene coding for triose phosphate isomerase, the pgk gene coding for 3-phosphoglycerate kinase, the zwf gene coding for glucose-6-phosphate dehydrogenase, the pyc gene coding for pyruvate carboxylase, the lysC gene coding for a feedback-resistant aspartate kinase, the lysE gene coding for lysine export, the horn gene coding for homoserine dehydrogenase, the ilvA gene coding for threonine dehydratase or the ilvA(Fbr) allele coding for a feedback-resistant threonine dehydratase, the ilvBN gene coding for acetohydroxy acid synthase, the ilvD gene coding for dihydroxy acid dehydratase, and the zwa1 gene coding for the Zwa1 protein.

PGPUB-DOCUMENT-NUMBER: 20020039766

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020039766 A1

TITLE: Nucleotide sequences coding for the pknD gene

PUBLICATION-DATE: April 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bathe, Brigitte	Salzkotten		DE	
Schroeder, Indra	Steinhagen		DE	
Farwick, Mike	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	

APPL-NO: 09/ 949971

DATE FILED: September 12, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60297266 20010612 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 44 948.4	2000DE-100 44 948.4	September 12, 2000
DE	101 20 094.3	2001DE-101 20 094.3	April 25, 2001

US-CL-CURRENT: 435/106, 435/194 , 435/252.3 , 435/320.1 , 536/23.2

ABSTRACT:

An isolated polynucleotide which contains a polynucleotide sequence selected from the group comprising:

- (a) a polynucleotide which is at least 70% identical to a polynucleotide coding for a polypeptide containing the amino acid sequence of SEQ ID No. 2,
  - (b) a polynucleotide coding for a polypeptide containing an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID No. 2,
  - (c) a polynucleotide which is complementary to the polynucleotides of (a) or (b), and
  - (d) a polynucleotide containing at least 15 consecutive nucleotides of the polynucleotide sequence of (a), (b), or (c),
- and a fermentation process for the preparation of L-amino acids using corynebacteria in which at least the pknD gene is amplified, and to the use, as hybridization probes, of polynucleotides containing the sequences according to the invention.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit to U.S. Provisional Application Serial No.60/297,266, filed Jun. 12, 2001 and identified herein by reference.

----- KWIC -----

Claims Text - CLTX (26):

25. The process of claim 15, wherein one or more endogenous genes selected from the following group are simultaneously amplified in the corynebacteria: the dapA gene coding for dihydrodipicolinate synthase, the gap gene coding for glyceraldehyde 3-phosphate dehydrogenase, the tpi gene coding for triose phosphate isomerase, the pgk gene coding for 3-phosphoglycerate kinase, the zwf gene coding for glucose-6-phosphate dehydrogenase, the pyc gene coding for pyruvate carboxylase, the lysC gene coding for a feedback-resistant aspartate kinase, the lysE gene coding for lysine export, the hom gene coding for homoserine dehydrogenase, the ilvA gene coding for threonine dehydratase or the ilvA(Fbr) allele coding for a feedback-resistant threonine dehydratase, the ilvBN gene coding for acetohydroxy acid synthase, the ilvD gene coding for dihydroxy acid dehydratase, and the zwa1 gene coding for the Zwa1 protein.

PGPUB-DOCUMENT-NUMBER: 20020006645

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020006645 A1

TITLE: Method for producing optically active compound

PUBLICATION-DATE: January 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hashimoto, Shin-Ichi	Tokyo		JP	
Katsumata, Ryoichi	Sendai-shi		JP	

APPL-NO: 09/ 764315

DATE FILED: January 19, 2001

RELATED-US-APPL-DATA:

child 09764315 A1 20010119

parent division-of 09092063 19980605 US GRANTED

parent-patent 6207427 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	150913/97	1997JP-150913/97	June 9, 1997

US-CL-CURRENT: 435/136, 435/252.3 , 435/252.33

ABSTRACT:

The present invention provides a method for industrially advantageously producing (S)-4-hydroxy-2-ketoglutaric acid and for producing compounds which are formed by biosynthesis from the precursor (S)-4-hydroxy-2-ketoglutaric acid, for example, for producing the compounds (2S,4S)-4-hydroxy-L-glutamic acid and (2S,4S)-4-hydroxy-L-proline, using a recombinant microorganism carrying a recombinant DNA harboring the DNA fragment encoding 4(S)-4-hydroxy-2-ketoglutaric acid aldolase gene.

----- KWIC -----

Detail Description Paragraph - DETX (30):

[0042] Examples of the biocatalyst having activity of converting 4(S)KHG into 4(S)HYP in the presence of the amino group donor include cells, a culture and processed cells of microorganisms having activity of converting 4(S)KHG into 4(S)HYP. Such microorganisms include microorganisms of genus *Escherichia* and *Corynebacterium*. More specifically, the microorganisms include strain ATCC 33625 of *Escherichia coli* K-12, which is prepared by modifying proBA gene (encoding proB and proA) coding for the enzyme of proline synthesis in *Escherichia coli* and then preparing plasmid pKSR25 carrying the resulting mutant proBA gene with reduced feed back inhibition, and thereafter introducing the plasmid into an *Escherichia coli* strain. More preferably, a mutant strain with a glutamic acid requirement is mentioned. Such a mutant strain can be



prepared by subjecting its parent strain to conventional mutagenesis technique, for example, N-methyl-N'-nitro-N-nitrosoguanidine (NTG), UV irradiation or .gamma. irradiation, coating the resulting strains on an appropriate agar plate medium, harvesting a grown mutant strain, and selecting a strain with glutamic acid requirement for the growth. In a case of a microorganism of Escherichia coli K-12, furthermore, a deletion mutant strain can also be produced by transduction. Such a microorganism includes NHK3/pKSR25 strain, which is prepared by first obtaining an isocitrate dehydrogenase deletion mutation (icd) of strain ATCC 33625 of Escherichia coli K-12 to obtain strain NHK3, and subsequently introducing pKSR25 into strain NHK3; such a microorganism also includes strain (NHK3/pKSR25+pKSR50), with plasmid pKSR50 additionally containing glutamate dehydrogenase and glucose-6-phosphate dehydrogenase having been introduced therein. A host microorganism with a glutamic acid requirement and with resistance to azetidine-2-carboxylic acid and proline analogs such as 3,4-dehydroproline and thioproline is more advantageously used. Such microorganism can be obtained by subjecting its parent strain to mutagenesis and transduction; additionally, the microorganism can be obtained by introducing a plasmid having proline analog resistance into the parent strain. More specifically, Escherichia coli strain NHK23/pKSR25+pKSR50 is mentioned. Escherichia coli strains NHK3/pKSR25+pKSR50 and Escherichia coli strain NHK23/pKSR25+pKSR50 were deposited with the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology in Japan on Apr. 16, 1997 as FERM BP-5922 and BP-5923, respectively, under the Budapest Treaty.

US-PAT-NO: 6689586

DOCUMENT-IDENTIFIER: US 6689586 B2

TITLE: Nucleotide sequences which code for the CcpA2 gene

DATE-ISSUED: February 10, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Moeckel; Bettina	Duesseldorf	N/A	N/A	DE
Kreutzer; Caroline	Melle	N/A	N/A	DE
Hermann; Thomas	Bielefeld	N/A	N/A	DE
Garwick; Mike	Bielefeld	N/A	N/A	DE
Marx; Achim	Bielefeld	N/A	N/A	DE
Pfefferle; Walter	Halle	N/A	N/A	DE

APPL-NO: 09/ 938642

DATE FILED: August 27, 2001

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
DE	100 42 053	August 26, 2000
DE	101 23 071	May 11, 2001

US-CL-CURRENT: 435/69.1, 435/252.3 , 435/252.32 , 435/320.1 , 536/23.1

ABSTRACT:

The invention relates to polynucleotides corresponding to the ccpA2 gene and which encode a CcpA2 catabolite control protein, methods of producing L-amino acids, and methods of screening for polynucleotides which encode proteins having CcpA2 catabolite control activity.

18 Claims, 1 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

----- KWIC -----

Detailed Description Text - DETX (50):

Thus, for example, the preparation of L-lysine, one or more of the genes chosen from the group the lysC gene which codes for a feed-back resistant aspartate kinase (Accession No. P26512; EP-B-0387527; EP-A-0699759), the dapA gene which codes for dihydrodipicolinate synthase (EP-B 0 197 335), the eno gene which codes for enolase (DE: 19947791.4), the zwf gene which codes for the zwf gene product (JP-A-09224661), the dapD gene which codes for tetrahydrodipicolinate succinylase (Wehrmann et al., Journal of Bacteriology 180, 3159-3165 (1998)), the dapE gene which codes for succinyldiaminopimelate desuccinylase (Wehrmann et al., Journal of Bacteriology 177: 5991-5993 (1995)), the gap gene which codes for glyceraldehyde 3-phosphate dehydrogenase (Eikmanns (1992). Journal of Bacteriology 174:6076-6086), the pyc gene which codes for pyruvate carboxylase (Peters-Wendisch et al.(Microbiology 144, 915-927 (1998))

the mqo gene which codes for malate:quinone oxidoreductase (Molenaar et al., European Journal of Biochemistry 254, 395-403 (1998)), the zwa1 gene which codes for the Zwa1 protein (DE: 19959328.0, DSM 13115) the lysE gene which codes for lysine export (DE-A-195 48 222) may at the same time be enhanced, in particular over-expressed.

US-PAT-NO: 6551795

DOCUMENT-IDENTIFIER: US 6551795 B1

TITLE: Nucleic acid and amino acid sequences relating to  
pseudomonas aeruginosa for diagnostics and therapeutics

DATE-ISSUED: April 22, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rubenfield; Marc J.	Framingham	MA	N/A	N/A
Nolling; Jork	Quincy	MA	N/A	N/A
Deloughery; Craig	Medford	MA	N/A	N/A
Bush; David	Somerville	MA	N/A	N/A

APPL-NO: 09/ 252991

DATE FILED: February 18, 1999

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is converted from U.S. provisional application Serial No. 60/074,788, filed Feb. 18, 1998 and U.S. provisional application Serial No. 60/094,190 filed Jul. 27, 1998.

US-CL-CURRENT: 435/69.1, 435/253.3 , 435/320.1 , 435/325 , 435/6 , 536/23.1  
, 536/23.7

ABSTRACT:

The invention provides isolated polypeptide and nucleic acid sequences derived from *Pseudomonas aeruginosa* that are useful in diagnosis and therapy of pathological conditions; antibodies against the polypeptides; and methods for the production of the polypeptides. The invention also provides methods for the detection, prevention and treatment of pathological conditions resulting from bacterial infection.

26 Claims, 0 Drawing figures

Exemplary Claim Number: 1

----- KWIC -----

Detailed Description Paragraph Table - DETL (78):

arabidopsis thaliana chromosome 1 yac yup8h12 complete sequence.) (nt: est gblatts1136 comes from this gene.) 23941542\_c3\_1617 2177 18748 336 111 100 -3 equine herpesvirus type 4 AF030027 (fn:very large tegument- EHV-4 protein) (de:equine herpes- virus 4 strain ns80567, complete genome.) (nt: counterpart of hsv-1 gene u136 and vzv gene 22) 16283583\_c3\_1619 2178 18749 480 159 125 -8 Klebsiella pneumoniae Contig519A GTC ORF with score 164 to: (ai:7000769991) (or: Pseudomonas aeruginosa) 35281530\_c3\_1621 2179 18750 453 150 91 -4 Holothuria tubulosa P14309 (sr:,sea cucumber) (de:sperm- specific protein phi-0) 35286466\_c3\_1624 2180 18751 981 326 111 -2 Mycobacterium bovis

BCG JC4743 (ec:2.3.1.85) 35283541\_c3\_1626 2181 18752 945 314 202 -14  
 Klebsiella pneumoniae Contig553A GTC ORF with score 202 to: (ai:7000763996)  
 (or: Pseudomonas aeruginosa) 3242807\_f1\_7 2182 18753 1557 518 1338 -136  
Corynebacterium sp. P40875 (ec:1.5.3.1) (de:sarcosine oxidase beta subunit.)  
 12995311\_f1\_8 2183 18754 414 137 260 -22 Corynebacterium sp. Q46336 (sr:p-1.)  
 (ec:1.5.3.1) (de: sarcosine oxidase delta subunit.) 14947525\_f1\_10 2184  
 18755 540 179 144 -9 Homo sapiens M74027 (sr:homo sapiens (tissue library:  
 lambda-gem-11 (stratagene)) bloo) (de:human mucin-2 gene, partial cds.)  
 10010457\_f1\_11 2185 18756 408 135 134 -8 Chlamydomonas reinhardtii S50755  
 strain UTEX 1061 22860841\_f1\_16 2186 18757 915 304 734 -72 Corynebacterium  
 sp. Q46339 (ec:3.5.1.10) (de:hydrolase)) 31678841\_f1\_18 2187 18758 804 267  
 104 -3 southern root-knot nematode S34665 (cl:unassigned collagens)  
 7117887\_f1\_19 2188 18759 966 321 331 -30 Escherichia coli P39173 (de:unknown  
 protein from 2d- page (spots t26/pr37)) 33798280\_f1\_22 2189 18760 2070 689  
 151 -8 Klebsiella pneumoniae Contig487A GTC ORF with score 567 to:  
 (ai:7000825229) (or: Enterobacter cloacae) 13006966\_f1\_24 2190 18761 651 216  
 124 -5 human herpesvirus type 6 U92288 (fn:helicase, helicase-primase HHV-6  
 complex) (de:human herpes- virus 6 serotype b putative major  
 immediate-earlygenes.) (nt:similar to hhy6a u86, region ie-b)  
 12554553\_f1\_27 2191 18762 918 305 102 -3 Aspergillus fumigatus Contig243 GTC  
 ORF with score 212 to: (ai:7000707570) (or: Plasmodium yoelii)  
 (de:plasmodium yoelii yoelii erythrocyte binding protein (maebi) gene,  
 complete cds.) (nt:maebi) 14352255\_f1\_34 2192 18763 486 161 279 -24  
 Acinetobacter sp. ADP1 AF009672 (de:acinetobacter sp. adp1 vanillate  
 demethylase region, vanillate demethylase (vanb) and vanillate demethylase  
 (vana) genes, completecds.) (nt:putative acetyl transferase; orf2)  
 12239757\_f1\_35 2193 18764 894 297 212 -15 Boreogadus saida U43200  
 (de:boreogadus saida anti- freeze glycopeptide afgp poly- protein  
 precursor gene, complete cds.) (nt:cleavage of polyprotein at conserved  
 spacers r or) 15729180\_f1\_39 2194 18765 477 158 111 -6 Enterococcus faecium  
 CONTIG321 GTC ORF with score 227 to: C (ai:7500727678) (or: Clostridium  
 acetobutylicum) 24428181\_f1\_45 2195 18766 1005 334 615 -60 no gb taxonomy  
 match AF012127 (de:thiobacillus intermedius k12 cbbr, ribulose  
 biphosphatocarboxylase/ oxygenase form ii (cbbm) and putative calvin  
 cycleprotein (cbbq) genes, complete cds.) (nt:up regulator of cbbm; calvin  
 cycle regulator of the) 23988800\_f1\_50 2196 18767 1518 505 1213 -123  
 Pseudomonas aeruginosa AF029673 (ec:1.1.1.49) (de: pseudomonas aeruginosa  
 hexr (hexr), glucose-6-phosphate1- dehydrogenase (zwf), and 2-  
 keto-3-deoxy-6-phospho- gluconatealdolase (cda) genes, complete cds.)  
 15722255\_f1\_54 2197 18768 1971 656 5207262\_f1\_60 2198 18769 2196 731 2446  
 -254 Serratia marcescens AF028736 (de:serratia marcescens site specific  
 recombinase (xerc)

US-PAT-NO: 6365381

DOCUMENT-IDENTIFIER: US 6365381 B2

TITLE: Method for producing optically active compound

DATE-ISSUED: April 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hashimoto; Shin-ichi	Machida	N/A	N/A	JP
Katsumata; Ryoichi	Sendai	N/A	N/A	JP

APPL-NO: 09/ 764315

DATE FILED: January 19, 2001

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional of Ser. No. 09/092,063, filed Jun. 5, 1998 now U.S. Pat. No. 6,207,427.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	9-150913	June 9, 1997

US-CL-CURRENT: 435/107, 435/252.33, 435/320.1

ABSTRACT:

The present invention provides a method for industrially advantageously producing (S)-4-hydroxy-2-ketoglutaric acid and for producing compounds which are formed by biosynthesis from the precursor (S)-4-hydroxy-2-ketoglutaric acid, for example, for producing the compounds (2S,4S)-4-hydroxy-L-glutamic acid and (2S,4S)-4-hydroxy-L-proline, using a recombinant microorganism carrying a recombinant DNA harboring the DNA fragment encoding 4(S)-4-hydroxy-2-ketoglutaric acid aldolase gene.

12 Claims, 4 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 3

----- KWIC -----

Detailed Description Text - DETX (30):

Examples of the biocatalyst having activity of converting 4(S)KHG into 4(S)HYP in the presence of the amino group donor include cells, a culture and processed cells of microorganisms having activity of converting 4(S)KHG into 4(S)HYP. Such microorganisms include microorganisms of genus *Escherichia* and *Corynebacterium*. More specifically, the microorganisms include strain ATCC 33625 of *Escherichia coli* K-12, which is prepared by modifying proBA gene (encoding proB and proA) coding for the enzyme of proline synthesis in

Escherichia coli and then preparing plasmid pKSR25 carrying the resulting mutant proBA gene with reduced feed back inhibition, and thereafter introducing the plasmid into an Escherichia coli strain. More preferably, a mutant strain with a glutamic acid requirement is mentioned. Such a mutant strain can be prepared by subjecting its parent strain to conventional mutagenesis technique, for example, N-methyl-N'-nitro-N-nitrosoguanidine (NTG), UV irradiation or .gamma. irradiation, coating the resulting strains on an appropriate agar plate medium, harvesting a grown mutant strain, and selecting a strain with glutamic acid requirement for the growth. In a case of a microorganism of Escherichia coli K-12, furthermore, a deletion mutant strain can also be produced by transduction. Such a microorganism includes NHK3/pKSR25 strain, which is prepared by first obtaining an isocitrate dehydrogenase deletion mutation (icd) of strain ATCC 33625 of Escherichia coli K-12 to obtain strain NHK3, and subsequently introducing pKSR25 into strain NHK3; such a microorganism also includes strain (NHK3/pKSR25+pKSR50), with plasmid pKSR50 additionally containing glutamate dehydrogenase and glucose-6-phosphate dehydrogenase having been introduced therein. A host microorganism with a glutamic acid requirement and with resistance to azetidine-2-carboxylic acid and proline analogs such as 3,4-dehydropoline and thioproline is more advantageously used. Such microorganism can be obtained by subjecting its parent strain to mutagenesis and transduction; additionally, the microorganism can be obtained by introducing a plasmid having proline analog resistance into the parent strain. More specifically, Escherichia coli strain NHK23/pKSR25+pKSR50 is mentioned. Escherichia coli strains NHK3/pKSR25+pKSR50 and Escherichia coli strain NHK23/pKSR25+pKSR50 were deposited with the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology in Japan on Apr. 16, 1997 as FERM BP-5922 and BP-5923, respectively, under the Budapest Treaty.

US-PAT-NO: 6207427

DOCUMENT-IDENTIFIER: US 6207427 B1

TITLE: Method for producing optically active compound

DATE-ISSUED: March 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hashimoto; Shin-ichi	Machida	N/A	N/A	JP
Katsumata; Ryoichi	Sendai	N/A	N/A	JP

APPL-NO: 09/ 092063

DATE FILED: June 5, 1998

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	9-150913	June 9, 1997

US-CL-CURRENT: 435/107, 435/106, 435/143, 435/252.3, 435/320.1

ABSTRACT:

The present invention provides a method for industrially advantageously producing (S)-4-hydroxy-2-ketoglutaric acid and for producing compounds which are formed by biosynthesis from the precursor (S)-4-hydroxy-2-ketoglutaric acid, for example, for producing the compounds (2S,4S)-4-hydroxy-L-glutamic acid and (2S,4S)-4-hydroxy-L-proline, using a recombinant microorganism carrying a recombinant DNA harboring the DNA fragment encoding 4(S)-4-hydroxy-2-ketoglutaric acid aldolase gene.

12 Claims, 4 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 3

----- KWIC -----

Detailed Description Text - DETX (30):

Examples of the biocatalyst having activity of converting 4(S)KHG into 4(S)HYP in the presence of the amino group donor include cells, a culture and processed cells of microorganisms having activity of converting 4(S)KHG into 4(S)HYP. Such microorganisms include microorganisms of genus *Escherichia* and *Corynebacterium*. More specifically, the microorganisms include strain ATCC 33625 of *Escherichia coli* K-12, which is prepared by modifying proBA gene (encoding proB and proA) coding for the enzyme of proline synthesis in *Escherichia coli* and then preparing plasmid pKSR25 carrying the resulting mutant proBA gene with reduced feed back inhibition, and thereafter introducing the plasmid into an *Escherichia coli* strain. More preferably, a mutant strain with a glutamic acid requirement is mentioned. Such a mutant strain can be prepared by subjecting its parent strain to conventional mutagenesis technique, for example, N-methyl-N'-nitro-N-nitrosoguanidine (NTG), UV irradiation or gamma irradiation, coating the resulting strains on an appropriate agar



plate medium, harvesting a grown mutant strain, and selecting a strain with glutamic acid requirement for the growth. In a case of a microorganism of Escherichia coli K-12, furthermore, a deletion mutant strain can also be produced by transduction. Such a microorganism includes NHK3/pKSR25 strain, which is prepared by first obtaining an isocitrate dehydrogenase deletion mutation (icd) of strain ATCC 33625 of Escherichia coli K-12 to obtain strain NHK3, and subsequently introducing pKSR25 into strain NHK3; such a microorganism also includes strain (NHK3/pKSR25+pKSR50), with plasmid pKSR50 additionally containing glutamate dehydrogenase and glucose-6-phosphate dehydrogenase having been introduced therein. A host microorganism with a glutamic acid requirement and with resistance to azetidine-2-carboxylic acid and proline analogs such as 3,4-dehydropoline and thioproline is more advantageously used. Such microorganism can be obtained by subjecting its parent strain to mutagenesis and transduction; additionally, the microorganism can be obtained by introducing a plasmid having proline analog resistance into the parent strain. More specifically, Escherichia coli strain NHK23/pKSR25+pKSR50 is mentioned. Escherichia coli strains NHK3/pKSR25+pKSR50 and Escherichia coli strain NHK23/pKSR25+pKSR50 were deposited with the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology in Japan on Apr. 16, 1997 as FERM BP-5922 and BP-5923, respectively, under the Budapest Treaty.

US-PAT-NO: 4090919

DOCUMENT-IDENTIFIER: US 4090919 A

TITLE: Water-insoluble tannin preparation for immobilization of proteins

DATE-ISSUED: May 23, 1978

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chibata; Ichiro	Suita	N/A	N/A	JA
Tosa; Tetsuya	Kyoto	N/A	N/A	JA
Mori; Takao	Takatsuki	N/A	N/A	JA
Watanabe; Taizo	Nagaokakyo		N/A	JA
Sano; Ryujiro	Toyonaka	N/A	N/A	JA
Matuo; Yuhsi	Suita	N/A	N/A	JA

APPL-NO: 05/ 760441

DATE FILED: January 19, 1977

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JA	51-8997	January 29, 1976
JA	51-102894	August 27, 1976
JA	51-131132	October 30, 1976

US-CL-CURRENT: 435/178, 210/679, 210/691, 426/422, 435/106, 435/137, 435/145, 435/177, 435/179, 435/183, 435/206, 435/68.1, 435/803, 435/815, 435/94, 435/99, 524/21, 530/368, 530/369, 530/386, 530/399, 530/415, 530/421, 530/813, 530/816, 536/120, 536/18.7, 536/32, 536/55.1, 536/56, 560/68

ABSTRACT:

A water-insoluble tannin preparation is obtained by covalent binding or physical adsorption of tannin onto a water-insoluble, hydrophilic carrier. The preparation has a specific affinity for proteins and can be used as an adsorbent for purification, isolation and/or separation of proteins (e.g., Enzymes, albumin, globulin, hormonal proteins) from a mixture of compounds. Further, the water-insoluble tannin preparation having a catalytically active enzyme absorbed thereon can be used as a heterogeneous catalyst to induce enzymatic reactions.

41 Claims, 0 Drawing figures

Exemplary Claim Number: 1,14,32,36

----- KWIC -----

Brief Summary Text - BSTX (32):

The water-insoluble tannin preparation of the present invention has a specific and unique affinity for proteins and can be used for immobilization or insolubilization of enzymes. That is, an immobilized enzyme is prepared by

adsorbing the enzyme physically on the water-insoluble tannin preparation. All of catalytically active enzymes are preferably used for this purpose. For example, enzymes which may be employed to produce immobilized preparations thereof include oxidoreductases such as amino acid oxidase, catalase, xanthin oxidase, glucose oxidase, glucose-6-phosphate dehydrogenase, glutamate dehydrogenase, cytochrome C oxidase, tyrosinase, lactate dehydrogenase, peroxidase, 6-phosphogluconate dehydrogenase and malate dehydrogenase; transferases such as aspartate acetyltransferase, aspartate aminotransferase, glycine aminotransferase, glutamic oxalacetic aminotransferase, glutamic pyruvic aminotransferase, creatine phosphokinase, histamine methyltransferase, pyruvate kinase, fructokinase, hexokinase .epsilon.-lysine acyltransferase and leucine aminopeptidase; hydrolases such as asparaginase, acetylcholinesterase, aminoacylase, amylase, arginase, L-arginine deiminase, invertase, urease, uricase, esterase, .beta.-galactosidase, kallikrein, chymotrypsin, trypsin, thrombin, naringinase, nucleotidase, papain, hyaluronidase, plasimin, pectinase, hesperidinase, pepsin, penicillinase, penicillin amidase, phospholipase, phosphatase, lactase, lipase, ribonuclease and renin; lyases such as aspartate decarboxylase, aspartase, citrate lyase, glutamate decarboxylase, histidine ammonia-lyase, phenylalanine ammonia-lyase, fumarase, fumarate hydratase and malate synthetase; isomerases such as alanine racemase, glucose isomerase, glucosephosphate isomerase, glutamate racemase, lactate racemase and methionine racemase and lygases such as asparagine synthetase.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4379	zwf or (g6p or glc6p or glucose-6-phosphate) adj (dh or dehydrogenase\$1) or g6pdh	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:20
L2	11	1 same corynebacter\$	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:40
L3	13	1 same ((amino adj acid or lysine or threonine or tryptophan or lys or thr or trp) near4 (biosynthes\$ or synthes\$10 or prepar\$10))\	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:40
L4	20	2 or 3	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:39
L5	608	poxb or pyruvate oxidase\$1 or pox adj b	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:39
L6	8	5 same corynebacter\$	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:40
L7	15	5 same ((amino adj acid or lysine or threonine or tryptophan or lys or thr or trp) near4 (biosynthes\$ or synthes\$10 or prepar\$10))\	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:41
L8	19	6 or 7	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:41

PGPUB-DOCUMENT-NUMBER: 20040063181

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040063181 A1

TITLE: Process for the preparation of L-amino acids using a  
gene encoding 6-phosphogluconate dehydrogenase

PUBLICATION-DATE: April 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Duncan, L. K.	Galway		IE	
McCormack, Ashling	Athlone		IE	
Stapleton, Cliona	Roscrea		IE	
Burke, Kevin	Galway		IE	
Mockel, Bettina	Bielefeld		DE	

APPL-NO: 10/ 686736

DATE FILED: October 17, 2003

RELATED-US-APPL-DATA:

child 10686736 A1 20031017

parent division-of 10078167 20020220 US PENDING

child 10078167 20020220 US

parent continuation-in-part-of 09531265 20000320 US ABANDONED

US-CL-CURRENT: 435/115, 435/252.3

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids. The process involves fermenting an L-amino acid producing coryneform bacteria in a culture medium, concentrating L-amino acid produced by the fermenting in the culture medium or in the cells of the bacteria, and isolating the L-amino acid produced. The bacteria has an overexpressed gene encoding 6-phosphogluconate dehydrogenase and a decreased or switched off gene encoding pyruvate oxidase. The L-amino acid may be L-lysine, L-threonine, L-isoleucine or L-tryptophan.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a continuation-in-part of U.S. application Ser. No. 09/531,265, filed on Mar. 20, 2000, the contents of which are incorporated by reference herein in their entirety.

----- KWIC -----

Detail Description Paragraph - DETX (150):

[0139] The vector pCR2.1poxBint mentioned in Example 10 was electroporated by the electroporation method of Tauch et al.(FEMS Microbiological Letters, 123:343-347 (1994)) in Corynebacterium glutamicum DSM 5715. Strain DSM 5715 is

an AEC-resistant lysine producer. The vector pCR2.1poxBint cannot replicate independently in DSM5715 and is retained only if it has integrated into the cell's chromosome. Selection of clones with pCR2.1poxBint integrated into the chromosome was carried out by plating out the electroporation batch on LB agar (Sambrook et al., Molecular Cloning: A Laboratory Manual. 2.sup.nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.), which had been supplemented with 15 mg/l kanamycin. For detection of the integration, the poxBint fragment was labeled with the Dig hybridization kit from Boehringer by the method of "The DIG System Users Guide for Filter Hybridization" of Boehringer Mannheim GmbH (Mannheim, Germany, 1993). Chromosomal DNA of a potential integrant was isolated by the method of Eikmanns et al. (Microbiology 140: 1817-1828 (1994)) and in each case cleaved with the restriction enzymes Sall, SacI and HindIII. The fragments formed were separated by agarose gel electrophoresis and hybridized at 68.degree. C. with the Dig hybridization kit from Boehringer. The plasmid pCR2.1poxBint mentioned in Example 9 had been inserted into the chromosome of DSM5715 within the chromosomal poxB gene. The strain was called DSM5715::pCR2.1poxBint.

Detail Description Paragraph - DETX (152):

Effect of Over-Expression of the gnd Gene with Simultaneous Elimination of the poxB Gene on the Preparation of Lysine

Claims Text - CLTX (2):

1. A process for the preparation of L-lysine, comprising: a) fermenting an L-lysine producing coryneform bacteria in a culture medium, the bacteria having at least an overexpressed gene encoding 6-phosphogluconate dehydrogenase; b) concentrating L-lysine produced by said fermenting in the culture medium or in the cells of the bacteria; and c) isolating the L-lysine produced; wherein intracellular activity of pyruvate oxidase encoded by a pyruvate oxidase gene is decreased or switched off in the bacteria.

Claims Text - CLTX (6):

5. A process for the preparation of an L-amino acid, comprising: a) fermenting an L-amino acid producing coryneform bacteria in a culture medium, the bacteria having at least an overexpressed gnd gene encoding 6-phosphogluconate dehydrogenase; b) concentrating L-amino acid produced by said fermenting in the culture medium or in the cells of the bacteria; and d) isolating the L-amino acid produced; wherein intracellular activity of pyruvate oxidase encoded by a pyruvate oxidase gene is decreased or switched off in the bacteria; and wherein the L-amino acid is selected from the group consisting of L-threonine, L-isoleucine and L-tryptophan.

PGPUB-DOCUMENT-NUMBER: 20040043458

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040043458 A1

TITLE: Coryneform bacteria which produce chemical compounds II

PUBLICATION-DATE: March 4, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bathe, Brigitte	Salzkotten		DE	
Kreutzer, Caroline	Melle		DE	
Mockel, Bettina	Dusseldorf		DE	
Thierbach, Georg	Bielefeld		DE	

APPL-NO: 10/ 358393

DATE FILED: February 5, 2003

RELATED-US-APPL-DATA:

child 10358393 A1 20030205

parent continuation-of PCT/EP02/08465 20020730 US UNKNOWN

non-provisional-of-provisional 60309877 20010806 US

US-CL-CURRENT: 435/91.1, 435/115 ; 435/252.3 , 435/320.1 , 435/471 , 435/472  
, 435/66 , 435/67

ABSTRACT:

The invention relates to coryneform bacteria which, instead of the singular copy of an open reading frame (ORF), gene or allele naturally present at the particular desired site (locus), have at least two copies of the open reading frame (ORF), gene or allele in question, preferably in tandem arrangement, and optionally at least a third copy of the open reading frame (ORF), gene or allele in question at a further gene site, and processes for the preparation of chemical compounds by fermentation of these bacteria.

[0001] This is a continuation of International Patent Appl. No. PCT/EP02/08465, filed Jul. 30, 2002, which claims priority to U.S. Prov. Appl. No. 60/309,877, filed Aug. 6, 2001.

----- KWIC -----

Claims Text - CLTX (38):

37. Process for the preparation of L-lysine according to claim 26, wherein the further gene site is one or more of the sites chosen from the group consisting of aecD, ccpA1, ccpA2, citA, citB, citE, fda, gluA, gluB, gluC, gluD, luxR, luxS, lysR1, lysR2, lysR3, menE, mgo, pck, pgi and poxB.

PGPUB-DOCUMENT-NUMBER: 20030219881

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030219881 A1

TITLE: Coryneform bacteria which produce chemical compounds I

PUBLICATION-DATE: November 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Brigitte, Bathe	Salzkotten		DE	
Caroline, Kreutzer	Melle		DE	
Bettina, Mockel	Dusseldorf		DE	
Georg, Thierbach	Bielefeld		DE	

APPL-NO: 10/ 358405

DATE FILED: February 5, 2003

RELATED-US-APPL-DATA:

child 10358405 A1 20030205

parent continuation-in-part-of PCT/EP02/08464 20020730 US UNKNOWN

non-provisional-of-provisional 60309878 20010806 US

US-CL-CURRENT: 435/106, 435/107 , 435/108 , 435/109 , 435/252.3 , 435/66  
, 435/67 , 435/91.1

ABSTRACT:

The invention relates to coryneform bacteria which have, in addition to at least one copy, present at the natural site (locus), of an open reading frame (ORF), gene or allele which codes for the synthesis of a protein or an RNA, in each case a second, optionally third or fourth copy of this open reading frame (ORF), gene or allele at in each case a second, optionally third or fourth site in a form integrated into the chromosome and processes for the preparation of chemical compounds by fermentation of these bacteria.

----- KWIC -----

Claims Text - CLTX (34):

33. Process for the preparation of L-lysine according to claim 26, wherein the particular second, optionally third or fourth site is a site chosen from the group consisting of aecD, ccpA1, ccpA2, citA, citB, citE, fda, gluA, gluB, gluc, gluD, luxR, luxS, lysR1, lysR2, lysR3, menE, mqo, pck, pgi and poxB.



PGPUB-DOCUMENT-NUMBER: 20030199045

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030199045 A1

TITLE: Process for the preparation of L-amino acids with  
amplification of the zwf gene

PUBLICATION-DATE: October 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Burke, Kevin	Galway		IE	
Sahm, Hermann	Julich		DE	
Eggeling, Lothar	Julich		DE	
Moritz, Bernd	Niederzier		DE	
Dunican, L. K.	Galway		IE	
McCormack, Ashling	Westmeath		IE	
Stapelton, Cliona	Roscrea		IE	
Mockel, Bettina	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	
Dunican, Rita	Galway		IE	

APPL-NO: 10/ 091342

DATE FILED: March 6, 2002

RELATED-US-APPL-DATA:

child 10091342 A1 20020306

parent continuation-in-part-of 09531269 20000320 US ABANDONED

US-CL-CURRENT: 435/115, 435/252.3 , 435/476

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids. The process involves fermenting an L-amino acid producing coryneform bacteria in a culture medium, concentrating L-amino acid in the culture medium or in the cells of the bacteria, and isolating the L-amino acid produced. The bacteria has an amplified gene encoding the Zwischenferment protein.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This is a continuation-in-part of U.S. application Ser. No. 09/531,269, filed Mar. 20, 2000, the contents of which are incorporated by reference herein in their entirety.

----- KWIC -----

Detail Description Paragraph - DETX (158):

[0159] The vector pCR2.1poxBint mentioned in Example 10 was electroporated by the electroporation method of Tauch et al.(FEMS Microbiological Letters, 123:343-347 (1994)) in Corynebacterium glutamicum DSM 5715. Strain DSM 5715 is an AEC-resistant lysine producer. The vector pCR2.1poxBint cannot replicate

independently in DSM5715 and is retained in the cell only if it has integrated into the chromosome of DSM 5715. Selection of clones with pCR2.1poxBint integrated into the chromosome was carried out by plating out the electroporation batch on LB agar (Sambrook et al., Molecular cloning: a laboratory manual. 2.sup.nd Ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.), which had been supplemented with 15 mg/l kanamycin. For detection of the integration, the poxBint fragment was labeled with the Dig hybridization kit from Boehringer by the method of "The DIG System Users Guide for Filter Hybridization" of Boehringer Mannheim GmbH (Mannheim, Germany, 1993). Chromosomal DNA of a potential integrant was isolated by the method of Eikmanns et al. (Microbiology 140: 1817-1828 (1994)) and in each case cleaved with the restriction enzymes Sall, SacI and HindIII. The fragments formed were separated by agarose gel electrophoresis and hybridized at 68.degree. C. with the Dig hybridization kit from Boehringer. The plasmid pCR2.1poxBint mentioned in Example 9 had been inserted into the chromosome of DSM5715 within the chromosomal poxB gene. The strain was called DSM5715::pCR2.1poxBint.

Detail Description Paragraph - DETX (160):

[0160] Effect of Over-Expression of the zwf Gene with Simultaneous Elimination of the poxB Gene on the Preparation of Lysine

Claims Text - CLTX (2):

1. A process for the preparation of L-lysine comprising: a) fermenting an L-lysine producing coryneform bacteria in a culture medium, the bacteria having at least an overexpressed zwf gene encoding the Zwischenferment protein; b) concentrating the L-lysine in the culture medium or in the cells of the bacteria; and c) isolating the L-lysine produced; wherein intracellular activity of pyruvate oxidase encoded by the poxB gene is decreased or switched off in the bacteria.

PGPUB-DOCUMENT-NUMBER: 20030175911

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175911 A1

TITLE: Process for the preparation of L-amino acids with  
amplification of the zwf gene

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hans, Stephen	Osnabruek		DE	
Bathe, Brigitte	Salzkotten		DE	
Reth, Alexander	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	
Kreutzer, Caroline	Melle		DE	
Mockel, Bettina	Dusseldorf		DE	

APPL-NO: 10/ 336049

DATE FILED: January 3, 2003

RELATED-US-APPL-DATA:

child 10336049 A1 20030103

parent continuation-in-part-of 10091342 20020306 US PENDING

child 10091342 20020306 US

parent continuation-in-part-of 09531269 20000320 US ABANDONED

US-CL-CURRENT: 435/115, 435/252.3

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids by the fermentation of coryneform bacteria. The process involves: fermenting an L-amino acid-producing bacteria in which at least the zwf gene is amplified; concentrating the L-amino acid in the medium or in the cells of the bacteria; and isolating the L-amino acid produced.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a continuation-in-part of U.S. Ser. No. 10/091,342, filed on Mar. 6, 2002, which is a continuation-in-part of U.S. Ser. No. 09/531,269, filed Mar. 20, 2000.

----- KWIC -----

Detail Description Paragraph - DETX (192):

[0191] Effect of Over-Expression of the zwf Gene with Simultaneous  
Elimination of the poxB Gene on the Preparation of Lysine

Claims Text - CLTX (2):

1. A process for the preparation of L-lysine by the fermentation of bacteria comprising the following steps: a) fermenting L-lysine producing bacteria in which a zwf gene encoding the Zwischenferment protein is overexpressed relative to the wild-type bacteria; b) concentrating L-lysine in the medium or in the cells of said coryneform bacteria; and c) isolating the L-lysine produced; wherein the intracellular activity of pyruvate oxidase encoded by the poxB gene is decreased or switched off.

PGPUB-DOCUMENT-NUMBER: 20030119154

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030119154 A1

TITLE: Process for the preparation of L-amino acids using a  
gene encoding 6-phosphogluconate dehydrogenase

PUBLICATION-DATE: June 26, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Dunican, L. K.	Galway		IE	
McCormack, Ashling	Athlone		IE	
Stapelton, Cliona	Roscrea		IE	
Burke, Kevin	Galway		IE	
Mockel, Bettina	Bielefeld		DE	

APPL-NO: 10/ 078167

DATE FILED: February 20, 2002

RELATED-US-APPL-DATA:

child 10078167 A1 20020220

parent continuation-in-part-of 09531265 20000320 US ABANDONED

US-CL-CURRENT: 435/115, 435/189 , 435/252.3 , 435/320.1 , 435/69.1  
, 536/23.2

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids. The process involves fermenting an L-amino acid producing coryneform bacteria in a culture medium, concentrating L-amino acid produced by the fermenting in the culture medium or in the cells of the bacteria, and isolating the L-amino acid produced. The bacteria has an overexpressed gene encoding 6-phosphogluconate dehydrogenase and a decreased or switched off gene encoding pyruvate oxidase. The L-amino acid may be L-lysine, L-threonine, L-isoleucine or L-tryptophan.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a continuation-in-part of U.S. application Ser. No. 09/531,265, filed on Mar. 20, 2000, the contents of which are incorporated by reference herein in their entirety.

----- KWIC -----

Detail Description Paragraph - DETX (158):

[0148] The vector pCR2.1poxBint mentioned in Example 10 was electroporated by the electroporation method of Tauch et al.(FEMS Microbiological Letters, 123:343-347 (1994)) in Corynebacterium glutamicum DSM 5715. Strain DSM 5715 is an AEC-resistant lysine producer. The vector pCR2.1poxBint cannot replicate independently in DSM5715 and is retained only if it has integrated into the cell's chromosome. Selection of clones with pCR2.1poxBint integrated into the

chromosome was carried out by plating out the electroporation batch on LB agar (Sambrook et al., Molecular Cloning: A Laboratory Manual. 2.sup.nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.), which had been supplemented with 15 mg/l kanamycin. For detection of the integration, the poxBint fragment was labeled with the Dig hybridization kit from Boehringer by the method of "The DIG System Users Guide for Filter Hybridization" of Boehringer Mannheim GmbH (Mannheim, Germany, 1993). Chromosomal DNA of a potential integrant was isolated by the method of Eikmanns et al. (Microbiology 140: 1817-1828 (1994)) and in each case cleaved with the restriction enzymes Sall, SacI and HindIII. The fragments formed were separated by agarose gel electrophoresis and hybridized at 68.degree. C. with the Dig hybridization kit from Boehringer. The plasmid pCR2.1poxBint mentioned in Example 9 had been inserted into the chromosome of DSM5715 within the chromosomal poxB gene. The strain was called DSM5715::pCR2.1poxBint.

Detail Description Paragraph - DETX (160):

Effect of Over-expression of the gnd Gene with Simultaneous Elimination of the poxB Gene on the Preparation of Lysine

Claims Text - CLTX (2):

1. A process for the preparation of L-lysine, comprising: a) fermenting an L-lysine producing coryneform bacteria in a culture medium, the bacteria having at least an overexpressed gene encoding 6-phosphogluconate dehydrogenase; b) concentrating L-lysine produced by said fermenting in the culture medium or in the cells of the bacteria; and c) isolating the L-lysine produced; wherein intracellular activity of pyruvate oxidase encoded by a pyruvate oxidase gene is decreased or switched off in the bacteria.

Claims Text - CLTX (6):

5. A process for the preparation of an L-amino acid, comprising: a) fermenting an L-amino acid producing coryneform bacteria in a culture medium, the bacteria having at least an overexpressed gnd gene encoding 6-phosphogluconate dehydrogenase; b) concentrating L-amino acid produced by said fermenting in the culture medium or in the cells of the bacteria; and d) isolating the L-amino acid produced; wherein intracellular activity of pyruvate oxidase encoded by a pyruvate oxidase gene is decreased or switched off in the bacteria; and wherein the L-amino acid is selected from the group consisting of L-threonine, L-isoleucine and L-tryptophan.

PGPUB-DOCUMENT-NUMBER: 20030109014

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109014 A1

TITLE: Process for the fermentative preparation of L-amino acids with amplification of the tkt gene

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Burke, Kevin	Newcastle		IE	
Duncan, L. K.	Bushy Park		IE	
Duncan, Rita	Galway		IE	
McCormack, Ashling	Athlone		IE	
Stapleton, Cliona	Roscrea		IE	
Mockel, Bettina	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	

APPL-NO: 10/ 143856

DATE FILED: May 14, 2002

RELATED-US-APPL-DATA:

child 10143856 A1 20020514

parent continuation-in-part-of 09986649 20011109 US ABANDONED

child 09986649 20011109 US

parent continuation-in-part-of 09528196 20000317 US ABANDONED

US-CL-CURRENT: 435/115, 435/106 , 435/189 , 435/193 , 435/252.3 , 435/320.1 , 435/69.1 , 536/23.2

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids by the fermentation of coryneform bacteria that over-express a gene encoding transketolase.

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application is a continuation-in-part of U.S. application Ser. No. 09/986,649, filed Nov. 9, 2001, which is a continuation-in-part of U.S. application Ser. No. 09/528,196, filed Mar. 17, 2000.

----- KWIC -----

Detail Description Paragraph - DETX (58):

[0133] The vector pCR2.1poxBint mentioned in Example 7, was electroporated by the method of Tauch et al. (FEMS Microbiol. Lett. 123:343-347 (1994)) in Corynebacterium glutamicum DSM 5715. Strain 5715 is an AEC-resistant lysine producer. The vector pCR2.1poxBint cannot replicate independently in DSM 5715.

Selection of clones with pCR2.1poxBint integrated into the chromosome was carried out by plating the electroporation batch on LB agar (Sambrook, et al., Molecular Cloning: A Laboratory Manual, 2.sup.nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.), which had been supplemented with 15 mg/l kanamycin. For detection of the integration, the poxBint fragment was labelled with the Dig hybridization kit from Boehringer by the method of "The Dig System Users Guide for Filter Hybridization" of Boehringer Mannheim GmbH (Mannheim, Germany, 1993). Chromosomal DNA of a potential integrant was isolated by the method of Eikmanns, et al. (Microbiology 140:1817-1828 (1994)) and in each case cleaved with the restriction enzymes Sall, SacI, and HindIII. The fragments formed were separated by agarose gel electrophoresis and hybridized at 68.degree. C. with the Dig hybridization kit from Boehringer. The plasmid pCR2.1poxBint mentioned in Example 9 has been inserted into the chromosome of DSM5715 within the chromosomal poxB gene. The strain was called DSM5715::pCR2.1poxBint.

Detail Description Paragraph - DETX (60):

[0134] Effect of Over-Expression of the tkt Gene with Simultaneous Elimination of the poxB Gene on the Preparation of Lysine

Claims Text - CLTX (5):

4. The process of claim 1, wherein said process is for the preparation of L-lysine and, in addition to over-expressing said endogenous gene coding for tkt, said bacteria have at least one endogenous gene that is attenuated, said endogenous gene being selected from the group consisting of: (a) the pck gene which codes for phosphoenol pyruvate carboxykinase; and (b) the poxB gene which codes for pyruvate oxidase. The process of any one of claims 1-4, wherein the over-expression or amplification of said gene coding for tkt or said additional endogenous gene is accomplished by transforming said bacteria with a plasmid vector carrying said gene coding for tkt or said additional endogenous gene.



PGPUB-DOCUMENT-NUMBER: 20030100080

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030100080 A1

TITLE: Nucleotide sequences which code for the sahH gene

PUBLICATION-DATE: May 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Farwick, Mike	Bielefeld		DE	
Huthmacher, Klaus	Gelnhausen		DE	
Brehme, Jennifer	Bielefeld		DE	
Pfefferle, Walter	Halle		DE	
Binder, Michael	Steinhagen		DE	
Greissinger, Dieter	Niddatal		DE	
Thierbach, Georg	Bielefeld		DE	

APPL-NO: 09/ 919854

DATE FILED: August 2, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60294277 20010531 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	DE 100 44 706.6	2000DE-DE 100 44 706.6	September 9, 2000
DE	DE 101 09 685.2	2001DE-DE 101 09 685.2	February 28, 2001

US-CL-CURRENT: 435/106, 435/252.33 , 435/320.1 , 435/69.1 , 536/23.2

ABSTRACT:

An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of

- polynucleotide which is at least 70% identical to a polynucleotide that codes for a polypeptide which comprises the amino acid sequence of SEQ ID No. 2,
- polynucleotide which codes for a polypeptide that comprises an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID No. 2,
- polynucleotide which is complementary to the polynucleotides of a) or b), and
- polynucleotide comprising at least 15 successive nucleotides of the polynucleotide sequence of a), b) or c),

and a process for the fermentative preparation of L-amino acids using coryneform bacteria, in which at least the sahH gene is present in enhanced form, and the use of polynucleotides which contain the sequences according to the invention as hybridization probes.

----- KWIC -----

Claims Text - CLTX (17):

17. The process as claimed in claim 10, wherein for the preparation of L-lysine or L-methionine, coryneform microorganisms are employed which have one or more attenuated genes selected from the group consisting of 17.1 the pck gene which codes for phosphoenol pyruvate carboxykinase, 17.2 the pgi gene which codes for glucose 6-phosphate isomerase, 17.3 the poxB gene which codes for pyruvate oxidase 17.4 the zwa2 gene which codes for the Zwa2 protein.

PGPUB-DOCUMENT-NUMBER: 20030017554

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030017554 A1

TITLE: Process for the fermentative preparation of L-amino acids using strains of the enterobacteriaceae family

PUBLICATION-DATE: January 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rieping, Mechthild	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	

APPL-NO: 10/ 076416

DATE FILED: February 19, 2002

RELATED-US-APPL-DATA:

child 10076416 A1 20020219

parent continuation-of 09987541 20011115 US ABANDONED

non-provisional-of-provisional 60283612 20010416 US

non-provisional-of-provisional 60248210 20001115 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	101 12 107.5	2001DE-101 12 107.5	March 14, 2001

US-CL-CURRENT: 435/106, 435/115 , 435/116 , 435/252.3

ABSTRACT:

A process for the fermentative preparation of an L-amino acid which entails the steps of:

- fermenting microorganisms of the Enterobacteriaceae family which produce the desired L-amino acid and in which at least the *poxB* gene or nucleotide sequences which code therefor are attenuated, in particular eliminated,
- concentrating the L-amino acid in the medium or in the cells of the bacteria, and
- isolating the L-amino acid.

----- KWIC -----

Detail Description Paragraph - DETX (36):

[0051] It may furthermore be advantageous for the production of L-amino acids, in particular L-threonine, with strains of the Enterobacteriaceae family to enhance one or more enzymes of the known threonine biosynthesis pathway or enzymes of anaplerotic metabolism or enzymes for the production of reduced nicotinamide adenine dinucleotide phosphate, in addition to the attenuation of the *poxB* gene.

Claims Text - CLTX (2):

1. A process for fermentatively preparing an L-amino acid, which comprises the steps of: a) fermenting microorganisms of the Enterobacteriaceae family which produce an L-amino acid and in which at least poxB gene or nucleotide sequences which code therefor are attenuated or eliminated; b) concentrating the L-amino acid in the medium or in the cells of the bacteria; and c) isolating the L-amino acid.

PGPUB-DOCUMENT-NUMBER: 20030017553

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030017553 A1

TITLE: Nucleotide sequences for transcriptional regulation in  
corynebacterium glutamicum

PUBLICATION-DATE: January 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Crafton, Corey M.	Decatur	IL	US	
Rayapati, P. John	Monticello	IL	US	

APPL-NO: 09/ 987763

DATE FILED: November 15, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60248219 20001115 US

US-CL-CURRENT: 435/106, 435/252.3 , 435/320.1 , 435/69.1 , 536/23.2

ABSTRACT:

The invention relates to isolated polynucleotides from *Corynebacterium glutamicum* which are useful in the regulation of gene expression. In particular, the invention relates to isolated polynucleotides comprising *C. glutamicum* promoters which may be used to regulate, i.e., either increase or decrease, gene expression. In certain embodiments, isolated promoter sequences of the present invention regulate gene expression through the use of exogenous or endogenous induction. The invention further provides recombinant vectors and recombinant cells comprising isolated polynucleotides of the present invention, preferably in operable association with heterologous genes. Also provided are methods of regulating bacterial gene expression comprising growth of a recombinant cell of the present invention. In particular, the present invention provides methods to regulate genes involved in amino acid production comprising growth of a recombinant cell of the present invention. In certain embodiments, the present invention provides methods of regulating gene expression in bacteria, particularly *Corynebacterium* species, especially of the genus *Corynebacterium*, comprising fermentation growth of a recombinant cell of the present invention, where metabolite concentrations, temperature, or oxygen levels are manipulated to regulate gene expression.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application 60/248,219, filed Nov. 15, 2000, which is incorporated herein by reference in its entirety.

----- KWIC -----

Detail Description Table CWU - DETL (1):

1TABLE 1A Nucleotide sequences that can be used to regulate gene

expression Seq. Regulatory I.D. NO: Gene\* Molecule.sup..dagger-dbl. 1 pta acetate 2 aceA acetate 3 aceB acetate 4 adh ethanol 5 aldB ethanol 6 poxB pyruvate 7 ldh pyruvate 8 amyB carbon 9 malZ carbon 10 bglX carbon 11 gam carbon 12 glgX carbon 13 hisD histidine 14 pyrR pyrimidine 15 purD purine 16 hrcA temperature 17 htpX temperature 18 dnaK temperature 19 ctc temperature 20 grpE temperature 21 clpB temperature 22 narA oxygen

Sequence I.D. NOs 1, 2, and 3 have been previously described. The remaining sequences were discovered in ADM's Corynebacterium glutamicum genome sequencing project. \*Putative genes regulated by sequence I.D. NOs 4-22 were determined by homology to genes identified in other organisms, e.g., Escherichia coli or Bacillus subtilis. .sup..dagger-dbl.Putative regulatory molecules associated with the regulatory regions of SEQ I.D. NOs 4-22 were determined by analogy to regulatory regions identified in other organisms.

PGPUB-DOCUMENT-NUMBER: 20020197605

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020197605 A1

TITLE: Novel Polynucleotides

PUBLICATION-DATE: December 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nakagawa, Satoshi	Tokyo		JP	
Mizoguchi, Hiroshi	Tokyo		JP	
Ando, Seiko	Tokyo		JP	
Hayashi, Mikiro	Tokyo		JP	
Ochiai, Keiko	Tokyo		JP	
Yokoi, Haruhiko	Tokyo		JP	
Tateishi, Naoko	Tokyo		JP	
Senoh, Akihiro	Tokyo		JP	
Ikeda, Masato	Tokyo		JP	
Ozaki, Akio	Hofu-shi		JP	

APPL-NO: 09/ 738626

DATE FILED: December 18, 2000

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	P. HEI 11-377484	1999JP-P. HEI 11-377484	December 16, 1999
JP	P. 2000-159162	2000JP-P. 2000-159162	April 7, 2000
JP	P. 2000-280988	2000JP-P. 2000-280988	August 3, 2000

US-CL-CURRENT: 435/6, 435/287.2 , 435/91.2

ABSTRACT:

Novel polynucleotides derived from microorganisms belonging to coryneform bacteria and fragments thereof, polypeptides encoded by the polynucleotides and fragments thereof, polynucleotide arrays comprising the polynucleotides and fragments thereof, recording media in which the nucleotide sequences of the polynucleotide and fragments thereof have been recorded which are readable in a computer, and use of them.

----- KWIC -----

Detail Description Table CWU - DETL (35):

2774814 2774110 705 prf:2222216A Thermotoga maritima drrA 42.0 72.7 231  
two-component system regulatory protein 2871 6371 2775689 2774937 753  
sp:TIPA\_STRLI Streptomyces lividans tipA 37.4 69.5 249 transcriptional  
activator 2872 6372 2776879 2775740 1140 prf:2419350A Arthrobacter sp. DK-38  
30.9 53.9 382 metal-activated pyridoxal enzyme or low specificity D-Thr  
aldolase 2873 6373 2778504 2776768 1737 gp:ECOPOXB8G\_1 Escherichia coli K12  
poxB 46.3 75.8 574 pyruvate oxidase 2874 6374 2778965 2780446 1482  
prf.2212334B Staphylococcus aureus plasmid 33.3 68.9 504 multidrug efflux  
protein pSK23 qacB 2875 6375 2780439 2780969 531 sp:YCDC\_ECOLI Escherichia  
coli K12 ycdC 30.4 68.5 92 transcriptional regulator 2876 6376 2780996

2782315 1320 pir:D70551 Mycobacterium tuberculosis 45.6 78.4 421 hypothetical  
 membrane protein H37Rv Rv2508c 2877 6377 2784481 2782340 2142 2878 6378  
 2785615 2784656 960 gp:AF096929\_2 Rhodococcus erythropolis SQ1 34.3 62.1 303  
 3-ketosteroid dehydrogenase kstD1 2879 6379 2786355 2785651 705  
 sp:ALSR\_BACSU Bacillus subtilis 168 alsR 37.1 69.0 232 transcriptional  
 regulator, LysR family 2880 6380 2787782 2788594 813 pir:C70982 Mycobacterium  
 tuberculosis 28.4 52.9 278 hypothetical protein H37Rv Rv3298c lpqC 2881 6381  
 2789399 2788587 813 pir:C69862 Bacillus subtilis 168 ykrA 26.7 55.6 288  
 hypothetical protein 2882 6382 2789935 2789477 459 2883 6383 2790152 2790550  
 399 pir:A45264 Oryctolagus cuniculus kidney 28.6 50.7 140 hypothetical protein  
 cortex rBAT 2884 6384 2790946 2792448 1503 pir:B70798 Mycobacterium  
 tuberculosis 36.0 64.0 464 hypothetical membrane protein H37Rv Rv3737 2885  
 6385 2792531 2792857 327 pir:S41307 Streptomyces griseus hrdB 32.3 50.3 155  
 transcription initiation factor sigma 2886 6386 2792873 2794327 1455  
 sp:TPS1\_SCHPO Schizosaccharomyces pombe 38.8 66.7 487 trehalose-6-phosphate  
 synthase tps1 2887 6387 2794300 2794812 513 2888 6388 2794870 2795637 768  
 sp:OTSB\_ECOLI Escherichia coli K12 otsB 27.4 57.6 245 trehalose-phosphatase  
 2889 6389 2796749 2795676 1074 sp:CCPA\_BACME Bacillus megaterium ccpA 24.7  
 60.2 344 glucose-resistance amylase regulator 2890 6390 2796865 2797806 942  
 sp:ZNUA\_HAEIN Haemophilus influenzae Rd 22.4 46.7 353 high-affinity zinc  
 uptake system HI0119 znuA protein 2891 6391 2797820 2798509 690  
 gp:AF121672\_2 Staphylococcus aureus 8325-4 31.4 63.2 223 ABC transporter mreA  
 2892 6392 2798837 2799391 555 pir:E70507 Mycobacterium tuberculosis 60.0 87.4  
 135 hypothetical membrane protein H37Rv Rv2060 2893 6393 2799535 2801034 1500  
 pir:A69426 Archaeoglobus fulgidus 23.4 52.5 303 transposase (ISA0963-5) 2894  
 6394 2801113 2801313 201 2895 6395 2803246 2801558 1689 gp:AF096929\_2  
 Rhodococcus erythropolis SQ1 32.1 62.0 561 3-ketosteroid dehydrogenase kstD1  
 2896 6396 2803996 2803250 747 2897 6397 2804691 2804074 618 pir:B72359  
 Thermotoga maritima MSB8 34.3 56.4 204 lipopolysaccharide biosynthesis bplA  
 protein or oxidoreductase or dehydrogenase 2898 6398 2805110 2804676 435  
 sp:MI2D\_BACSU Bacillus subtilis 168 idh or iolG 35.2 69.5 128 dehydrogenase or  
 myo-inositol 2- dehydrogenase 2899 6399 2805967 2805113 855 sp:SHIA\_ECOLI  
 Escherichia coli K12 shiA 30.5 67.5 292 shikimate transport protein 2900 6400  
 2806441 2806016 426 sp:SHIA\_ECOLI Escherichia coli K12 shiA 43.1 80.8 130  
 shikimate transport protein 2901 6401 2807252 2806599 654 gp:SC5A7\_19  
 Streptomyces coelicolor A3(2) 32.6 55.7 212 transcriptional regulator  
 SC5A7.19c 2902 6402 2808364 2807426 939 sp:PT56\_YEAST Saccharomyces  
 cerevisiae 22.8 47.3 334 ribosomal RNA ribose methylase or YOR201C PET56  
 tRNA/rRNA methyltransferase 2903 6403 2809778 2808399 1380 sp:SYC\_ECOLI  
 Escherichia coli K12 cysS 42.2 68.8 464 cysteinyl-tRNA synthetase 2904 6404  
 2811806 2809824 1983 prf:2511335C Lactococcus lactis sacB 47.0 77.0 668 PTS  
 system, enzyme II sucrose protein (sucrose-specific IIBC component) 2905  
 6405 2813258 2811960 1299 gp:AF205034\_4 Clostridium acetobutylicum 35.3 56.9  
 473 sucrose 6-phosphate hydrolase or ATCC 824 scrB sucrase 2906 6406 2814037  
 2813279 759 sp:NAGB\_ECOLI Escherichia coli K12 nagB 38.3 69.4 248  
 glucosamine-6-phosphate isomerase 2907 6407 2815232 2814081 1152  
 sp:NAGA\_VIBFU Vibrio furnissii SR1514 manD 30.2 60.3 368  
 N-acetylglucosamine-6-phosphate deacetylase 2908 6408 2815458 2816393 936  
 sp:DAPA\_ECOLI Escherichia coli K12 dapA 28.2 62.1 298 dihydrodipicolinate  
 synthase 2909 6409 2816409 2817317 909 sp:GLK\_STRCO Streptomyces coelicolor  
 A3(2) 28.7 57.6 321 glucokinase SC6E10.20c glk 2910 6410 2817363 2818058  
 696 prf:2516292A Clostridium perfringens NCTC 36.4 68.6 220  
 N-acetylmannosamine-6-phosphate 8798 nanE epimerase 2911 6411 2818313 2818137  
 177 2912 6412 2819564 2818350 1215 sp:NANH\_MICVI Micromonospora viridifaciens  
 24.8 50.3 439 sialidase precursor ATCC 31146 nadA 2913 6413 2820285 2819557  
 729 gp:AF181498\_1 Rhizobium etli ansR 26.6 57.2 222 L-asparagine permease  
 operon repressor 2914 6414 2820584 2822191 1608 gp:BFU64514\_1 Bacillus  
 firmus OF4 dppA 22.5 51.4 560 dipeptide transporter protein or heme-binding  
 protein 2915 6415 2822387 2823337 951 sp:DPPB\_BACFI Bacillus firmus OF4 dappB



31.9 64.3 342 dipeptide transport system permease protein 2916 6416 2824274  
 2825341 1068 sp:OPPD\_BACSU *Bacillus subtilis* 168 oppD 46.5 78.3 314  
 oligopeptide transport ATP-binding protein 2917 6417 2825341 2826156 816  
 sp:OPPF\_LACLA *Lactococcus lactis* oppF 43.4 78.7 258 oligopeptide transport  
 ATP-binding protein 2918 6418 2826835 2826215 621 sp:RHTB\_ECOLI *Escherichia*  
*coli* K12 rhtB 28.5 62.7 193 homoserine/homoserin lactone efflux protein or  
 lysE type translocator 2919 6419 2826922 2827404 483 prf:2309303A  
*Bradyrhizobium japonicum* lrp 31.0 66.2 142 leucine-responsive regulatory  
 protein 2920 6420 2827817 2827458 360 2921 6421 2828383 2827904 480  
 pir:C70607 *Mycobacterium tuberculosis* 55.9 86.2 152 hypothetical protein H37Rv  
 Rv3581c 2922 6422 2829146 2828379 768 sp:Y18T\_MYCTU *Mycobacterium*  
*tuberculosis* 46.4 71.5 235 hypothetical protein H37Rv Rv3582c 2923 6423  
 2829749 2829156 594 pir:H70803 *Mycobacterium tuberculosis* 73.3 91.1 157  
 transcription factor H37Rv Rv3583c 2924 6424 2830057 2830779 723  
 prf:2214304A *Mycobacterium tuberculosis* 43.5 70.0 223 two-component system  
 response H37Rv Rv3246c mtrA regulator 2925 6425 2830779 2831894 1116  
 sp:BAES\_ECOLI *Escherichia coli* K12 baeS 29.3 67.7 341 two-component system  
 sensor histidine kinase 2926 6426 2832085 2832666 582 2927 6427 2832790  
 2834181 1392 sp:RADA\_ECOLI *Escherichia coli* K12 radA 41.5 74.3 463 DNA repair  
 protein RadA 2928 6428 2834188 2835285 1098 sp:YACK\_BACSU *Bacillus subtilis*  
 168 yackK 40.3 73.3 345 hypothetical protein 2929 6429 2835969 2835283 687  
 pir:D70804 *Mycobacterium tuberculosis* 29.4 53.3 231 hypothetical protein  
 H37Rv Rv3587c 2930 6430 2837499 2836048 1452 gp:PPU96338\_1 *Pseudomonas putida*  
 NCIMB 59.5 85.1 471 p-hydroxybenzaldehyde 9866 plasmid pRA4000 dehydrogenase  
 2931 6431 2837737 2837591 147 2932 6432 2838576 2837956 621 pir:T08204  
*Chlamydomonas reinhardtii* ca1 36.7 66.2 210 mitochondrial carbonate  
 dehydratase beta 2933 6433 2838643 2839521 879 gp:AF121797\_1 *Streptomyces*  
*antibioticus* IMRU 48.4 70.7 283 A/G-specific adenine glycosylase 3720 mutY  
 2934 6434 2839562 2840716 1155 2935 6435 2841063 2840758 306 2936 6436  
 2841075 2841848 774 gp:AB009078\_1 *Brevibacterium saccharolyticum* 99.2 99.6 258  
 L-2,3-butanediol dehydrogenase 2937 6437 2842130 2842453 324 2938 6438  
 2842493 2843233 741 2939 6439 2843405 2843716 312 2940 6440 2843722 2843432  
 291 pir:E70552 *Mycobacterium tuberculosis* 48.5 69.1 97 hypothetical protein  
 H37Rv Rv3592 2941 6441 2845139 2845558 420 GSP:Y29188 *Pseudomonas aeruginosa*  
 57.0 63.0 99 virulence factor ORF24222 2942 6442 2845889 2846101 213  
 GSP:Y29193 *Pseudomonas aeruginosa* 54.0 55.0 72 virulence factor ORF25110  
 2943 6443 2846186 2846506 321 GSP:Y29193 *Pseudomonas aeruginosa* 74.0 75.0 55  
 virulence factor ORF25110 2944 6444 2846940 2844166 2775 sp:MECB\_BACSU  
*Bacillus subtilis* 168 mecB 58.5 86.2 832 ClpC adenosine triphosphatase/  
 ATP-binding proteinase 2945 6445 2847229 2848659 1431 gp:AB035643\_1 *Bacillus*  
*cereus* ts-4 impdh 37.1 70.2 469 inosine monophosphate dehydrogenase 2946  
 6446 2848769 2849779 1011 pir:JC6117 *Rhodococcus rhodochrous* nitR 24.7 62.7  
 316 transcription factor 2947 6447 2850031 2851815 1785 sp:PH2M\_TRICU  
*Trichosporon cutaneum* ATCC 33.5 60.9 680 phenol 2-monooxygenase 46490 2948  
 6448 2852017 2853732 1716 2949 6449 2853769 2855709 1941 2950 6450 2855795  
 2857516 1722 2951 6451 2859044 2859205 162 2952 6452 2859055 2857613 1443  
 gp:AF237667\_1 *Corynebacterium glutamicum* 100.0 100.0 481 lincomycin resistance  
 protein lmrB 2953 6453 2860145 2859195 951 pir:G70807 *Mycobacterium*  
*tuberculosis* 26.7 55.8 240 hypothetical protein H37Rv Rv3517 2954 6454  
 2862082 2860505 1578 gp:AB012100\_1 *Bacillus stearothermophilus* lysS 41.7 71.2  
 511 lysyl-tRNA synthetase 2955 6455 2862929 2862132 798 gp:CGPAN\_2  
*Corynebacterium glutamicum* 29.9 52.6 268 pantoate-beta-alanine ligase

PGPUB-DOCUMENT-NUMBER: 20020155555

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020155555 A1

TITLE: Nucleotide sequences which code for the pgsA2 gene

PUBLICATION-DATE: October 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nampoothiri K., Madhavan	Kerala		IN	
Mockel, Bettina	Dusseldorf		DE	
Pfefferte, Walter	Halle		DE	
Eggeling, Lothar	Julich		DE	
Sahm, Hermann	Julich		DE	

APPL-NO: 09/ 855835

DATE FILED: May 16, 2001

RELATED-US-APPL-DATA:

child 09855835 A1 20010516

parent continuation-in-part-of 09577855 20000525 US ABANDONED

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 21 829.6	2000DE-100 21 829.6	May 4, 2000

US-CL-CURRENT: 435/115, 424/93.4 , 435/106 , 514/44

ABSTRACT:

The invention relates to a genetically modified coryneform bacterium, the pgsA2 gene of which is amplified, and an isolated polynucleotide which codes for CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase from coryneform bacteria, and also a method for the fermentative preparation of L-amino acids with amplification of the pgsA2 gene in the bacteria and the use of the polynucleotide as a primer or hybridization probe.

RELATED APPLICATION DATA

[0001] This application is a Continuation-In-Part of co-pending U.S. patent appln. Ser. No. 09/577,855 filed May 25, 2000, which application claims priority under 35 U.S.C. sctn. 119 from German Patent Appln. No. 10021829.6, filed in Germany on May 4, 2000. The above-identified U.S. patent application and German patent application are entirely incorporated herein by reference. The invention provides genetically modified coryneform bacteria, nucleotide sequences which code for CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase and methods for the fermentative preparation of amino acids, in particular L-lysine, using coryneform bacteria in which the pgsA2 gene, which codes for CDP-diacylglycerol-glycerol-3-phosphate 3-phosphatidyltransferase (EC 2.7.8.5), is amplified. All references cited herein are expressly incorporated by reference. Incorporation by reference is also designated by the term "I.B.R." following any citation.

----- KWIC -----

Claims Text - CLTX (23):

22. The method as claimed in claim 13, wherein for the preparation of L-lysine, bacteria in which one or more genes selected from the group consisting of a) the pck gene which codes for phosphoenol pyruvate carboxykinase, b) the pgi gene which codes for glucose 6-phosphate isomerase, and c) the poxB gene which codes for pyruvate oxidase, is attenuated at the same time are said bacteria fermented.

PGPUB-DOCUMENT-NUMBER: 20020081660

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020081660 A1

TITLE: In vitro macromolecule biosynthesis methods using  
exogenous amino acids and a novel ATP regeneration  
system

PUBLICATION-DATE: June 27, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Swartz, James R.	Menlo Park	CA	US	
Kim, Dong-Myung	Palo Alto	CA	US	

APPL-NO: 09/ 948815

DATE FILED: September 7, 2001

RELATED-US-APPL-DATA:

child 09948815 A1 20010907

parent continuation-of PCT/US00/07095 20000315 US UNKNOWN

non-provisional-of-provisional 60125463 19990322 US

US-CL-CURRENT: 435/69.1, 435/252.33

ABSTRACT:

Compositions and methods are provided for the enhanced in vitro synthesis of polypeptides. In order to improve the performance of in vitro protein synthesis reactions, metabolic inhibitors, or manipulation of a source organism, is used to diminish or avoid the action of enzymes responsible for undesirable amino acids production or depletion. A homeostatic system may be used for production of ATP, where the required high energy phosphate bonds are generated in situ, e.g. through coupling with an oxidation reaction. The homeostatic energy source will typically lack high energy phosphate bonds itself, and will therefore utilize free phosphate in the reaction mix during generation of ATP. The homeostatic energy source is provided in combination with an enzyme that catalyzes the creation of high energy phosphate bonds and with an enzyme that can use that high energy phosphate bond to regenerate ATP.

CROSS REFERENCE

[0001] This application is a Continuation of International Application Number PCT/US00/07095 filed Mar. 15, 2000, which claims benefit of United States application Ser. No. 09/270,814 filed Mar. 17, 1999, now issued U.S. Pat. No. 6,168,931 and U.S. Provisional Application Serial No. 60/125,463 filed Mar. 22, 1999, all of which are incorporated herein by reference.

----- KWIC -----

Detail Description Paragraph - DETX (93):

[0109] With aspartic acid and asparagine formation, the consequences are even more serious. These amino acids are formed from oxaloacetate which, in turn, is derived from PEP (FIG. 9). For the PEP system, this is a direct drain of the energy source. For the pyruvate system, the formation of these amino acids indicates that pyruvate is being converted to PEP. This will decrease the amount of pyruvate available for the pyruvate oxidase reaction. However, even more serious is the realization that this conversion requires the conversion of ATP to AMP. For every mole of PEP that is generated and used for amino acid synthesis, two moles of ATP and one mole of pyruvate are lost.

PGPUB-DOCUMENT-NUMBER: 20020072098

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020072098 A1

TITLE: Process for the fermentative preparation of L-amino acids using coryneform bacteria

PUBLICATION-DATE: June 13, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ziegler, Petra	Aachen		DE	
Eggeling, Lothar	Julich		DE	
Sahm, Hermann	Julich		DE	
Thierbach, Georg	Bielefeld		DE	
Pfefferle, Walter	Halle		DE	

APPL-NO: 09/ 731826

DATE FILED: December 8, 2000

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	199 59 329.9	1999DE-199 59 329.9	December 9, 1999

US-CL-CURRENT: 435/106, 435/252.3

ABSTRACT:

A process for the preparation of L-amino acids, in which the following steps are carried out,

- fermenting the desired L-amino acid-producing bacteria in which at least the glyA gene is attenuated, in particular by removal of the natural promoter, and optionally
- concentrating the desired product in the medium or in the cells of the bacteria and
- isolating the L-amino acid, and optionally bacteria in which further genes of the biosynthesis pathway of the desired L-amino acid are additionally amplified are employed, or bacteria in which the metabolic pathways which reduce the formation of the desired L-amino acid are at least partly eliminated are employed, and nucleotide sequences of the lacI-tac-5'glyA or lacI-tac-glyA unit.

----- KWIC -----

Claims Text - CLTX (11):

10. Process according to claim 1, wherein for the preparation of L-threonine, bacteria in which one or more genes chosen from the group consisting of: 1) the pck gene which codes for phosphoenol pyruvate carboxykinase, and or 2) the poxB gene which codes for pyruvate oxidase is/are attenuated at the same time the bacteria are fermented.

PGPUB-DOCUMENT-NUMBER: 20020042107

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020042107 A1

TITLE: Nucleotide sequences which code for the fadD15 gene

PUBLICATION-DATE: April 11, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nampoothiri K., Madhavan	Kerala	IN	US	
Mockel, Bettina	Dusseldorf	DE		
Pfefferle, Walter	Halle	DE		
Eggeling, Lothar	Julich	DE		
Sahm, Hermann	Julich	DE		

APPL-NO: 09/ 855750

DATE FILED: May 16, 2001

RELATED-US-APPL-DATA:

child 09855750 A1 20010516

parent continuation-in-part-of 09577848 20000525 US ABANDONED

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 21 831.8	2000DE-100 21 831.8	May 4, 2000

US-CL-CURRENT: 435/115, 435/252.3 , 435/6 , 536/23.2 , 536/24.3

ABSTRACT:

The invention relates to a genetically modified coryneform bacterium, the fadD15 gene of which is amplified, and an isolated polynucleotide which codes for acyl-CoA synthase from coryneform bacteria, and also a method for the fermentative preparation of L-amino acids with amplification of the fadD15 gene in the bacteria and the use of the polynucleotide as a primer or hybridization probe.

RELATED APPLICATION DATA

[0001] This application is a Continuation-In-Part of co-pending U.S. patent appln. Ser. No. 09/577,848 filed May 25, 2000, which application claims priority under 35 U.S.C. sctn. 119 from German Patent Appln. No. 10021831.8, filed in Germany on May 4, 2000. The above-identified U.S. patent application and German patent application are entirely incorporated herein by reference. The invention provides genetically modified coryneform bacteria, nucleotide sequences which code for for acyl-CoA synthase and a method for the fermentative preparation of amino acids, in particular L-lysine, using coryneform bacteria in which the fadD15 gene, which codes for acyl-CoA synthase, is amplified. All references cited herein are expressly incorporated by reference. Incorporation by reference is also designated by the term "I.B.R." following any citation.

----- KWIC -----

Claims Text - CLTX (23):

22. A method as claimed in claim 13, wherein for the preparation of L-lysine, bacteria in which one or more genes selected from the group consisting of a) the pck gene which codes for phosphoenol pyruvate carboxykinase, b) the pgi gene which codes for glucose 6-phosphate isomerase, and c) the poxB gene which codes for pyruvate oxidase, is or are attenuated at the same time are fermented.



PGPUB-DOCUMENT-NUMBER: 20020042105

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020042105 A1

TITLE: Nucleotide sequences coding for the pknB gene

PUBLICATION-DATE: April 11, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bathe, Brigitte	Saltzkotten		DE	
Hans, Stephan	Osnabrueck		DE	
Farwick, Mike	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	

APPL-NO: 09/ 949970

DATE FILED: September 12, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60297250 20010612 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 44 912.3	2000DE-100 44 912.3	September 12, 2000
DE	101 20 095.1	2001DE-101 20 095.1	April 25, 2001

US-CL-CURRENT: 435/106, 435/183, 435/252.3, 435/320.1, 536/23.2

ABSTRACT:

An isolated polynucleotide which contains a polynucleotide sequence selected from the group comprising:

- (a) a polynucleotide which is at least 70% identical to a polynucleotide coding for a polypeptide containing the amino acid sequence of SEQ ID No. 2,
  - (b) a polynucleotide coding for a polypeptide containing an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID No. 2,
  - (c) a polynucleotide which is complementary to the polynucleotides of (a) or (b), and
  - (d) a polynucleotide containing at least 15 consecutive nucleotides of the polynucleotide sequence of (a), (b) or (c),
- and a fermentation process for the preparation of L-amino acids using corynebacteria in which at least the pknB gene is amplified, and to the use, as hybridization probes, of polynucleotides containing the sequences according to the invention.

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims benefit to U.S. Provisional Application Ser. No. 60/297,250, filed on Jun. 12, 2001, and incorporated herein by reference.

----- KWIC -----

Claims Text - CLTX (27):

26. The process of claim 15, wherein one or more genes selected from the following group are simultaneously attenuated in the corynebacteria: the pck gene coding for phosphoenol pyruvate carboxykinase, the pgi gene coding for glucose-6-phosphate isomerase, the poxB gene coding for pyruvate oxidase, and the zwa2 gene coding for the Zwa2 protein.

PGPUB-DOCUMENT-NUMBER: 20020039766

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020039766 A1

TITLE: Nucleotide sequences coding for the pknD gene

PUBLICATION-DATE: April 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bathe, Brigitte	Salzkotten		DE	
Schroeder, Indra	Steinhagen		DE	
Farwick, Mike	Bielefeld		DE	
Hermann, Thomas	Bielefeld		DE	

APPL-NO: 09/ 949971

DATE FILED: September 12, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60297266 20010612 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
DE	100 44 948.4	2000DE-100 44 948.4	September 12, 2000
DE	101 20 094.3	2001DE-101 20 094.3	April 25, 2001

US-CL-CURRENT: 435/106, 435/194 , 435/252.3 , 435/320.1 , 536/23.2

ABSTRACT:

An isolated polynucleotide which contains a polynucleotide sequence selected from the group comprising:

- (a) a polynucleotide which is at least 70% identical to a polynucleotide coding for a polypeptide containing the amino acid sequence of SEQ ID No. 2,
  - (b) a polynucleotide coding for a polypeptide containing an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID No. 2,
  - (c) a polynucleotide which is complementary to the polynucleotides of (a) or (b), and
  - (d) a polynucleotide containing at least 15 consecutive nucleotides of the polynucleotide sequence of (a), (b), or (c),
- and a fermentation process for the preparation of L-amino acids using corynebacteria in which at least the pknD gene is amplified, and to the use, as hybridization probes, of polynucleotides containing the sequences according to the invention.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit to U.S. Provisional Application Serial No.60/297,266, filed Jun. 12, 2001 and identified herein by reference.

----- KWIC -----

Claims Text - CLTX (27):

26. The process of claim 15 wherein one or more genes selected from the following group are simultaneously attenuated in the corynebacteria: the pck gene coding for phosphoenol pyruvate carboxykinase, the pgi gene coding for glucose-6-phosphate isomerase, the poxB gene coding for pyruvate oxidase, and the zwa2 gene coding for the Zwa2 protein.

US-PAT-NO: 6596516

DOCUMENT-IDENTIFIER: US 6596516 B2

TITLE: Process for the fermentative preparation of L-amino acids using coryneform bacteria

DATE-ISSUED: July 22, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ziegler; Petra	Aachen	N/A	N/A	DE
Eggeling; Lothar	Julich	N/A	N/A	DE
Sahm; Hermann	Julich	N/A	N/A	DE
Thierbach; Georg	Bielefeld	N/A	N/A	DE
Pfefferle; Walter	Halle	N/A	N/A	DE

APPL-NO: 09/ 731826

DATE FILED: December 8, 2000

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
DE	199 59 329	December 9, 1999

US-CL-CURRENT: 435/106, 435/175, 435/243, 435/252.1, 435/252.3, 435/260, 435/320.1, 435/41, 435/440, 435/471, 435/476, 435/477, 536/23.1, 536/24.1

ABSTRACT:

A process for the preparation of L-amino acids, in which the following steps are carried out, a) fermenting the desired L-amino acid-producing bacteria in which at least the glyA gene is attenuated, in particular by removal of the natural promoter, and optionally b) concentrating the desired product in the medium or in the cells of the bacteria and c) isolating the L-amino acid,

and optionally bacteria in which further genes of the biosynthesis pathway of the desired L-amino acid are additionally amplified are employed, or bacteria in which the metabolic pathways which reduce the formation of the desired L-amino acid are at least partly eliminated are employed, and nucleotide sequences of the lacI-tac-5'glyA or lacI-tac-glyA unit.

12 Claims, 1 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

----- KWIC -----

Claims Text - CLTX (7):

7. The process according to claim 1, wherein for the preparation of L-threonine, bacteria in which one or more genes selected from the group consisting of: 1) the pck gene which codes for phosphoenol pyruvate carboxykinase, and 2) the poxB gene which codes for pyruvate oxidase is/are

attenuated at the same time the bacteria are fermented.

US-PAT-NO: 6337191

DOCUMENT-IDENTIFIER: US 6337191 B1

TITLE: Vitro protein synthesis using glycolytic intermediates  
as an energy source

DATE-ISSUED: January 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Swartz; James	Menlo Park	CA	N/A	N/A
Kim; Dong-Myung	Palo Alto	CA	N/A	N/A

APPL-NO: 09/ 621339

DATE FILED: July 21, 2000

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application 60/145,438, filed Jul. 23, 1999; and is a continuation-in-part of International Application PCT/US00/07095, Filed Mar. 15, 2000; which claims priority to U.S. Provisional Application No. 60/125,463, filed Mar. 22, 1999.

US-CL-CURRENT: 435/68.1, 435/6

ABSTRACT:

Compositions and methods are provided for the enhanced in vitro synthesis of biological molecules where ATP is required for synthesis. Of particular interest is the synthesis of polymers, e.g. nucleic acids, polypeptides, and complex carbohydrates. Glycolytic intermediates or glucose are used as an energy source, in combination with added NADH or NAD<sup>sup.+</sup>.

17 Claims, 6 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6

----- KWIC -----

Detailed Description Text - DETX (74):

With aspartic acid and asparagine formation, the consequences are even more serious. These amino acids are formed from oxaloacetate which, in turn, is derived from PEP. For a PEP system, this is a direct drain of the energy source. For the pyruvate system, the formation of these amino acids indicates that pyruvate is being converted to PEP. This will decrease the amount of pyruvate available for the pyruvate oxidase reaction. However, even more serious is the realization that this conversion requires the conversion of ATP to AMP. For every mole of PEP that is generated and used for amino acid synthesis, two moles of ATP and one mole of pyruvate are lost.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4379	zwf or (g6p or glc6p or glucose-6-phosphate) adj (dh or dehydrogenase\$1) or g6pdh	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:20
L2	11	1 same corynebacter\$	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:40
L3	13	1 same ((amino adj acid or lysine or threonine or tryptophan or lys or thr or trp) near4 (biosynthes\$ or synthes\$10 or prepar\$10))\	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:40
L4	20	2 or 3	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:39
L5	608	poxb or pyruvate oxidase\$1 or pox adj b	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:39
L6	8	5 same corynebacter\$	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:40
L7	15	5 same ((amino adj acid or lysine or threonine or tryptophan or lys or thr or trp) near4 (biosynthes\$ or synthes\$10 or prepar\$10))\	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:41
L8	19	6 or 7	US-PGPUB; USPAT	ADJ	OFF	2004/06/07 14:41